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ARTICLE

# Perineal Powder Use and Risk of Ovarian Cancer

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**Background** Case-control studies have reported an increased risk of ovarian cancer among talc users; however, the only cohort study to date found no association except for an increase in serous invasive ovarian cancers. The purpose of this analysis was to assess perineal powder use and risk of ovarian cancer prospectively in the Women's Health Initiative Observational Study cohort.

**Methods** Perineal powder use was assessed at baseline by self-report regarding application to genitals, sanitary napkins, or diaphragms and duration of use. The primary outcome was self-reported ovarian cancer centrally adjudicated by physicians. Cox proportional hazard regression was used to estimate risk, adjusting for covariates, including person-time until diagnosis of ovarian cancer (n = 429), death, loss to follow-up, or September 17, 2012. All statistical tests were two-sided.

**Results** Among 61 576 postmenopausal women, followed for a mean of 12.4 years without a history of cancer or bilateral oophorectomy, 52.6% reported ever using perineal powder. Ever use of perineal powder (hazard ratio $[HR]_{adj}$ = 1.06, 95% confidence interval [CI] = 0.87 to 1.28) was not associated with risk of ovarian cancer compared with never use. Individually, ever use of powder on the genitals ($HR_{adj}$ = 1.12, 95% CI = 0.92 to 1.36), sanitary napkins ($HR_{adj}$ = 0.95, 95% CI = 0.76 to 1.20), or diaphragms ($HR_{adj}$ = 0.92, 95% CI = 0.68 to 1.23) was not associated with risk of ovarian cancer compared with never use, nor were there associations with increasing durations of use. Estimates did not differ when stratified by age or tubal ligation status.

**Conclusion** Based on our results, perineal powder use does not appear to influence ovarian cancer risk.

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In 2013, it is estimated that there will be 22 240 new cases of ovarian cancer and 14 030 ovarian cancer deaths in the United States (US) alone (1). Since the 1960s, there has been speculation that the use of perineal powder is associated with ovarian cancer. In 2006, the International Agency for Research on Cancer (IARC) reviewed studies examining perineal powder use and ovarian cancer and classified talc as a possible carcinogen (2,3). The proportion of US women ever using talc powder on the perineum was estimated in 2001 to be approximately 40% (4), whereas 52% reported ever use of perineal powder in 1993–1998 within the Women's Health Initiative (WHI) (5).

The primary proposed mechanism linking perineal powder use to ovarian cancer is an inflammatory response (6). Talc particulates from perineal application have been shown to migrate to the ovaries (6), disrupting the surface ovarian epithelial tissue leading to entrapment of the talc particles within inclusion cysts (7). Furthermore, tubal ligation and/or hysterectomy, which would eliminate the pathway of talc particulates to the ovaries, are associated with reduced ovarian cancer risk (6).

A meta-analysis examining the risk of ovarian cancer among ever perineal powder users vs non-users showed odds ratios (ORs) of 1.40 (95% confidence interval [CI] = 1.29 to 1.52) for population-based case-control, 1.12 (95% CI = 0.92 to 1.36) for hospital based case-control, and 1.35 (95% CI = 1.26 to 1.46) for all case-control studies (2). More recently, a large pooled analysis found that ever use of perineal powder increased epithelial ovarian cancer risk by 24% compared with non-use (OR = 1.24, 95% CI = 1.15 to 1.33) (8). Increased risk was associated with invasive serous, endometrioid, clear cell, and borderline serous subtypes of epithelial ovarian cancer (8). However, when looking at the lifetime number of applications of perineal powder, there was no statistically significant trend for increasing applications, attributed to difficulty in recalling details of frequency and duration of perineal powder use (8).

To date there has only been one prospective study conducted examining perineal powder use and risk of ovarian cancer (9). In the Nurses' Health Study (NHS) cohort, no overall association was found between ever use of perineal powder and epithelial ovarian cancer (relative risk [RR] = 1.09, 95% CI = 0.86 to 1.37) or serous ovarian cancers (RR = 1.26, 95% CI = 0.94 to 1.69) (9). However, there was a 40% (95% CI = 1.02 to 1.91) increase in risk for serous

invasive ovarian cancer with ever perineal powder use, which comprises 86% of serous ovarian cancers in this cohort (9).

Limitations of recall bias and misclassification make it difficult to determine the true relationship between perineal powder (10), a commonly used cosmetic product, and ovarian cancer, a disease with poor survival and few known modifiable risk factors. The prior prospective cohort study, which should not be affected by recall bias, had no information on duration of use limiting interpretation. Here we expand on the available evidence by assessing perineal powder use and risk of ovarian cancer in the Women's Health Initiative Observational Study (WHI-OS). The WHI-OS is a large cohort that collected information on several application areas of perineal powder use and their respective durations of use.

## Methods

### Study Population

The WHI-OS enrolled 93 676 women from 40 clinical centers across the United States from 1993 to 1998 (11). Women were eligible if they were aged 50 to 79 at enrollment, postmenopausal, and planned to reside in the area for at least three years (11). Women were excluded from the WHI-OS if they were participating in another clinical trial, unlikely to survive three years due to medical conditions, or had conditions that would interfere with study participation (11). Participants completed annual mailed questionnaires to update information on risk factors and outcomes, including ovarian cancer (11). Written informed consent was obtained from participants, and all clinical centers were approved by their respective institutional review boards (11). The current analysis was approved by the University of Massachusetts, Amherst Human Subjects Review Committee.

For this analysis, participants were additionally excluded if they reported a bilateral oophorectomy or an unknown number of ovaries at baseline (n = 20 960), a history of any cancer at baseline except nonmelanoma skin cancer (n = 10 622), or were missing exposure or follow up information (n = 516). After applying the exclusion criteria, 61 576 participants with 429 adjudicated incident ovarian cancer cases remained.

### Exposure Ascertainment

Perineal powder use was assessed via self-report at baseline. Participants were asked, "Have you ever used powder on your private parts (genital areas)?" Those who responded yes further indicated the duration of use with the following possible responses: less than 1 year, 1–4 years, 5–9 years, 10–19 years, or 20 or more years. For persons that reported ever use of a diaphragm, participants were asked, "Did you ever use powder on your diaphragm?" and those who responded yes further indicated duration. The third category evaluated was "Did you ever use powder on a sanitary napkin or pad?" with those responding yes also reporting duration. Each area of application variable was assessed dichotomously and the duration of use, collapsed into fewer categories because of small numbers, was assessed categorically as never, 9 years or less, or 10 or more years. A combined ever perineal powder variable and duration variable for any powder use was created; where ever use was defined as report of ever use of any of the three application categories, never was report of never use for all three categories, and duration was the maximum duration reported of any single area of application, because we could not exclude the possibility that applications were concurrent. Lastly, all possible combinations of the three application areas were assessed.

### Outcome Ascertainment

Ovarian cancer cases were initially self-reported by participants in the WHI-OS on annual questionnaires. Medical records, including hospital discharge summaries and pathology reports, were requested for each self-reported case and adjudicated by a physician at the local Clinical Center and then centrally by the WHI's Clinical Coordinating Center (11).

### Covariate Ascertainment

Potential covariates considered included age, race, education, alcohol servings per week, smoking status, metabolic equivalent (MET) hours per week of recreational physical activity, Body Mass Index (BMI), and self-reported family history of ovarian or breast cancer. Reproductive factors considered were age at menarche, age at menopause, age at first birth, age at last birth, parity, breastfeeding duration, history of tubal ligation, history of hysterectomy, history of irregular cycles, history of endometriosis, duration of oral contraceptive use, and duration of postmenopausal hormone use. All covariates were from baseline and were not updated.

### Statistical Analysis

To estimate the association between perineal powder use and ovarian cancer, proportional hazard regression models were used. Participants contributed person-time until diagnosis of ovarian cancer, death, loss to follow-up, or September 17, 2012, whichever came first. Participants with other cancers were still considered at risk for ovarian cancer and were not censored at the time of other cancer diagnoses. Information on incident oophorectomy during follow-up was not available and thus participants were not censored in this analysis. The proportional hazards assumption was tested using weighted Schoenfeld residuals.

Covariates were included in the adjusted model according to purposeful selection, where covariates with Wald *P* values of .25 or less in age-adjusted models were entered into an initial multivariable model and then each covariate was subsequently tested individually via likelihood ratio tests in order of decreasing Wald *P* values. Variables that had *P* values of .10 or less during the backwards elimination were kept in the model until a parsimonious model was obtained. Additional variables shown in previous literature (8,9) but not statistically significant in our population were also included in the final multivariable model. Lastly, family history of breast cancer and personal history of endometriosis did not change estimates and were not included in the final multivariable model.

Models fitted included the following independent variables: 1) combined ever perineal powder use, 2) ever powder use by application area (ie, applied to genitals, applied to diaphragm, or applied to sanitary napkins), 3) duration of use by application area, and 4) application area combinations (ie, genital only, diaphragm only, sanitary napkin only, genital and sanitary napkin, genital and diaphragm, diaphragm and sanitary napkin, and all three areas of application). For duration models, test for trend was used to evaluate linear trends across duration categories by modeling the

categories as a continuous variable in the multivariable regression models.

Because powder particles may not reach the ovaries due to tubal ligation and because previous studies have shown a stronger association between powder use and ovarian cancer in women without tubal ligation (4), we separately examined women without tubal ligation. We also stratified by age at baseline, because older women may have had more potential for exposure to talc contaminated with asbestos. Additionally, associations by ovarian cancer histological subtype were evaluated. All analyses were performed using Stata v.12.1 (StataCorp, College Station, TX) and two-sided *P* values of .05 or less were considered statistically significant.

## Results

The average age of the participants at baseline was 63.3 years. Participants were followed for a mean of 12.4 years; never powder users were followed for a mean of 12.2 years (range = 0.12 to 17.9 years) and ever powder users were followed for a mean of 12.6 years (range = 0.03 to 18.0). The majority of the participants were white (83.7%), had less than a college degree (56.1%), and were overweight/obese (57.2%). Approximately half (52.6%) of the population reported ever use of perineal powder. Ever powder users were heavier (27.5 kg/m$^2$ vs 26.5 kg/m$^2$, $P < .0001$) and were more likely to have used oral contraceptives (44% vs 36%, $P < .0001$) and/or diaphragms (50.8% vs 37.3 %, $P < .0001$) than never users (Table 1).

Use of powder on the genitals was associated with a 12% increase in the multivariable-adjusted hazard ratio of ovarian cancer ($HR_{adj}$ = 1.12, 95% CI = 0.92 to 1.36), though this was not statistically significant (Table 2). Use of powder on sanitary napkins ($HR_{adj}$ = 0.95, 95% CI = 0.76 to 1.20) or diaphragms ($HR_{adj}$ = 0.92, 95% CI = 0.68 to 1.23) also was not associated with risk. Duration of powder use on the genitals, sanitary napkins, or on the diaphragm was not associated with ovarian cancer; $P_{trend}$ for years of use: .67, .69, and .67 respectively. Combined ever powder use from any of the three application areas did not show an association with ovarian cancer risk ($HR_{adj}$ = 1.06, 95% CI = 0.87 to 1.28). For combined duration of use, which was the longest duration of use among the three areas of application, there was no evidence of an association with risk of ovarian cancer [$P_{trend}$ for years of use: .77]. Use of powder on genitals, the most common application area, for 20 or more years was not associated with increased risk of ovarian cancer compared with never users ($HR_{adj}$ = 1.10, 95% CI = 0.82 to 1.48). In a sensitivity analysis, invasive serous ovarian cancer risk was not increased ($HR_{adj}$ = 0.96, 95% CI = 0.65 to 1.41), even in women reporting durations of use greater than 10 years.

There was no evidence of an association between perineal powder use and ovarian cancer risk by category of application (Table 3). Combined ever powder use was not associated with individual subtypes of ovarian cancer (Table 4). The multivariable-adjusted hazard ratio for serous ovarian cancer was 1.16 (95% CI = 0.88 to 1.53). Additionally, duration of combined ever powder use was also not shown to be associated with any subtype of ovarian cancer (results not shown).

The associations of combined ever powder use and ovarian cancer did not statistically differ by tubal ligation status (results not shown). When stratified by age group at baseline, hazard estimates also did not statistically differ ($P_{interaction}$ = .37); $HR_{adj}$ for younger than 50 to 59 years = 1.29, 95% CI = 0.91 to 1.82; $HR_{adj}$ for those 60 to 69 years = 0.94, 95% CI = 0.70 to 1.26; and $HR_{adj}$ for those 70 to 79 years = 1.01, 95% CI = 0.68 to 1.48. When restricted to only whites or to those who had never used oral contraceptives, results were again unchanged.

**Table 1.** Characteristics of postmenopausal women according to perineal powder use status (n = 61 285): Women's Health Initiative Observational Study, 1993–2012

| | Never perineal powder use | Ever perineal powder use |
|---|---|---|
| **Characteristic, n (%)** | **n = 29 066** | **n = 32 219** |
| Race | | |
| White | 24 006 (82.6) | 27 336 (84.8) |
| Nonwhite | 4991 (17.2) | 4811 (14.9) |
| Body mass index category, kg/m$^2$ | | |
| <25.0 | 13 056 (44.9) | 12 461 (38.7) |
| 25.0–29.9 | 9734 (33.5) | 10 799 (33.5) |
| 30.0 + | 5935 (20.4) | 8571 (26.6) |
| Smoking status | | |
| Never | 15 347 (52.8) | 15 621 (48.5) |
| Past | 11 481 (39.5) | 14 339 (44.5) |
| Current | 1912 (6.6) | 1881 (5.8) |
| Duration of oral contraceptive use, y | | |
| Never | 17 877 (61.5) | 17 954 (55.7) |
| <5 | 6241 (21.5) | 7858 (24.4) |
| 5 to <10 | 2528 (8.7) | 3270 (10.2) |
| 10 to <15 | 1650 (5.7) | 2125 (6.6) |
| 15+ | 760 (2.6) | 1005 (3.1) |
| Diaphragm use | 10 826 (37.3) | 16 353 (50.8) |
| Tubal ligation | 4929 (17.0) | 5901 (18.3) |
| Hysterectomy | 6878 (23.7) | 8285 (25.7) |
| Family history of ovarian cancer | 606 (2.1) | 660 (2.1) |
| Parity | | |
| 0 | 3687 (12.7) | 3769 (11.7) |
| 1–2 | 9773 (33.6) | 11 585 (36.0) |
| 3–4 | 11 101 (38.2) | 12 609 (39.1) |
| 5+ | 4365 (15.0) | 4098 (12.7) |
| Age at last birth, y | | |
| Never had term pregnancy | 6219 (21.4) | 6260 (19.4) |
| < 20 | 210 (0.7) | 324 (1.0) |
| 20–29 | 9143 (31.5) | 11480 (35.6) |
| 30+ | 13 011 (44.8) | 13 668 (42.4) |
| Duration of postmenopausal hormone use, y | | |
| Never | 13 381 (46.0) | 13 880 (43.1) |
| <5 | 6498 (22.4) | 7546 (23.4) |
| 5 to <10 | 3783 (13.0) | 4567 (14.2) |
| 10 to <15 | 2688 (9.3) | 3128 (9.7) |
| 15+ | 2716 (9.3) | 3097 (9.6) |

## Discussion

In this large prospective study, ever perineal powder use was not associated with ovarian cancer risk, nor was it associated with ovarian cancer when assessed by area of application, duration of use, or ovarian cancer subtype. While many case-control studies have shown an approximately 24–40% increase in risk of ovarian cancer (2,8) for powder users, we did not find evidence of this association in our large, prospective analysis.

The meta-analysis of 20 case-control studies by Langseth and colleagues found a 35% increase in the odds of epithelial ovarian

**Table 2.** Age and multivariable-adjusted hazard ratios of ovarian cancer by area of perineal powder application (n = 61 576): Women's Health Initiative Observational Study, 1993–2012

| Variable | No. of cases | Person-years | Age-adjusted HR (95% CI) | $P_{trend}$ † | Multivariable HR* (95% CI) | $P_{trend}$ † |
|---|---|---|---|---|---|---|
| Powder use on genitals | | | | | | |
| Never | 247 | 457 855 | 1.0 (referent) | .63 | 1.0 (referent) | .67 |
| Ever‡ | 181 | 304 867 | 1.13 (0.93 to 1.37) | | 1.12 (0.92 to 1.36) | |
| Less than 9 years | 112 | 173 118 | 1.24 (0.99 to 1.55) | | 1.23 (0.98 to 1.54) | |
| 10 or more years | 68 | 129 647 | 0.98 (0.75 to 1.29) | | 0.98 (0.75 to 1.29) | |
| Powder use on sanitary napkins | | | | | | |
| Never | 336 | 590 351 | 1.0 (referent) | .70 | 1.0 (referent) | .69 |
| Ever‡ | 93 | 172 712 | 0.96 (0.76 to 1.21) | | 0.95 (0.76 to 1.20) | |
| Less than 9 years | 62 | 114 305 | 0.98 (0.75 to 1.28) | | 0.96 (0.73 to 1.26) | |
| 10 or more years | 30 | 56 174 | 0.93 (0.64 to 1.35) | | 0.95 (0.65 to 1.37) | |
| Powder use on diaphragm | | | | | | |
| Never | 373 | 661 239 | 1.0 (referent) | .78 | 1.0 (referent) | .67 |
| Ever‡ | 52 | 97 714 | 0.94 (0.70 to 1.25) | | 0.92 (0.68 to 1.23) | |
| Less than 9 years | 35 | 67 468 | 0.93 (0.66 to 1.32) | | 0.91 (0.64 to 1.30) | |
| 10 or more years | 17 | 29 202 | 0.99 (0.61 to 1.60) | | 0.95 (0.58 to 1.56) | |
| Combined ever powder use§ | | | | | | |
| Never | 197 | 361 583 | 1.0 (referent) | .67 | 1.0 (referent) | .77 |
| Ever‡ | 232 | 404 983 | 1.07 (0.89 to 1.30) | | 1.06 (0.87 to 1.28) | |
| Less than 9 years | 135 | 228 931 | 1.12 (0.90 to 1.39) | | 1.09 (0.88 to 1.36) | |
| 10 or more years | 97 | 173 307 | 1.03 (0.81 to 1.31) | | 1.02 (0.80 to 1.30) | |

* Adjusted for: Age (continuous), race (white, nonwhite, missing), oral contraceptive duration in years (never, <5, 5 to <10, 10 to <15, 15+, missing), hormone replacement therapy duration in years (never, <5, 5 to <10, 10 to <15, 15+, missing), family history (yes, no, missing), age (y) at last birth (never, <20, 20 to <30, 30+, missing), body mass index in kg/m$^2$ (<25.0, 25.0 to <30.0, 30.0+, missing), smoking (never, past, current, missing), tubal ligation (yes, no, missing), and parity (0, 1 to 2, 3 to 4, 5+, children, missing).

† Hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated in cox proportional hazard regression models; $P_{trend}$ was estimated by modeling categories as continuous. All statistical tests were two-sided.

‡ Person-years may not add up; duration information was missing for some.

§ Combined ever powder use is the longest duration of use among the applications to genitals, sanitary napkins, and diaphragms.

**Table 3.** Age and multivariable-adjusted hazard ratios for ovarian cancer by combined categories of powder use (n = 61 576): Women's Health Initiative Observational Study, 1993–2012

| Variable | No. of cases | Person-years | Age-adjusted HR* (95% CI) | Multivariable HR* (95% CI) |
|---|---|---|---|---|
| Powder Type Used | | | | |
| No powder | 193 | 355 523 | 1.0 (referent) | 1.0 (referent) |
| Only genital powder | 96 | 158 130 | 1.14 (0.90 to 1.46) | 1.13 (0.88 to 1.45) |
| Only diaphragm powder | 19 | 42 367 | 0.82 (0.51 to 1.32) | 0.80 (0.50 to 1.29) |
| Only sanitary napkin powder | 28 | 50 051 | 1.04 (0.70 to 1.54) | 1.01 (0.68 to 1.50) |
| Genital and sanitary napkin powder | 55 | 96 173 | 1.09 (0.80 to 1.47) | 1.08 (0.80 to 1.46) |
| Genital and diaphragm powder | 24 | 29 858 | 1.49 (0.98 to 2.28) | 1.45 (0.95 to 2.23) |
| Diaphragm and sanitary napkin powder | 4 | 6858 | 1.06 (0.40 to 2.86) | 1.02 (0.38 to 2.74) |
| Genital, diaphragm, and sanitary napkin powder | 5 | 18 331 | 0.51 (0.21 to 1.24) | 0.50 (0.21 to 1.22) |

* Hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated in cox proportional hazard regression models. All statistical tests were two-sided. Multivariable HR adjusted for: age (continuous), race (white, nonwhite, missing), oral contraceptive duration in years (never, <5, 5 to <10, 10 to <15, 15+, missing), hormone replacement therapy duration in years (never, <5, 5 to <10, 10 to <15, 15+, missing), family history (yes, no, missing), age (y) at last birth (never, <20, 20 to <30, 30+, missing), body mass index in kg/m$^2$ (<25.0, 25.0 to <30.0, 30.0+, missing), smoking (never, past, current, missing), tubal ligation (yes, no, missing), and parity (0, 1 to 2, 3 to 4, 5+, children missing).

cancer among ever perineal powder users compared to never-users (2), and the pooled analysis of eight case-control studies by Terry and colleagues found a 24% increase in the same group (8). Langseth and colleagues did not assess dose-response or risk among subtypes of ovarian cancer (2). Terry and colleagues assessed lifetime applications of perineal powder and found no statistically significant trend with increasing lifetime applications (8). This corroborates our results that there was no statistically significant risk with increasing duration of perineal powder use, though they were able to capture both frequency and duration (8), whereas we only had duration. Terry and colleagues found elevated risks for invasive serous, borderline serous, endometrioid, and clear cell subtypes of ovarian cancer (8), which we did not observe. One potential reason that case-control studies have found slight increases in risk is the potential for an overestimation of the true association due to recall bias, because the participants are aware of their ovarian cancer status when reporting powder

**Table 4.** Age and multivariable-adjusted hazard ratios for combined ever powder use by subtype of ovarian cancer (n = 61 576): Women's Health Initiative Observational Study, 1993–2012

| Variable | No. of cases | Person-years | Age-adjusted HR* (95% CI) | Multivariable HR* (95% CI) |
|---|---|---|---|---|
| Serous† | | | | |
| Never | 87 | 355 523 | 1.0 (referent) | 1.0 (referent) |
| Ever | 117 | 404 983 | 1.18 (0.89 to 1.56) | 1.16 (0.88 to 1.53) |
| Serous Invasive | | | | |
| Never | 80 | 355 523 | 1.0 (referent) | 1.0 (referent) |
| Ever | 105 | 404 983 | 1.16 (0.87 to 1.55) | 1.13 (0.84 to 1.51) |
| Mucinous | | | | |
| Never | 12 | 355 523 | 1.0 (referent) | 1.0 (referent) |
| Ever | 13 | 404 983 | 0.98 (0.44 to 2.14) | 1.03 (0.47 to 2.27) |
| Endometrioid | | | | |
| Never | 13 | 355 523 | 1.0 (referent) | 1.0 (referent) |
| Ever | 20 | 404 983 | 1.39 (0.69 to 2.79) | 1.29 (0.64 to 2.61) |
| Other | | | | |
| Never | 47 | 355 523 | 1.0 (referent) | 1.0 (referent) |
| Ever | 54 | 404 983 | 1.04 (0.71 to 1.54) | 1.04 (0.70 to 1.54) |

* Hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated in cox proportional hazard regression models. All statistical tests were two-sided. Multivariable HR adjusted for: age (continuous), race (white, nonwhite, missing), oral contraceptive duration in years (never, <5, 5 to <10, 10 to <15, 15+, missing), hormone replacement therapy duration in years (never, <5, 5 to <10, 10 to <15, 15+, missing), family history (yes, no, missing), age (y) at last birth (never, <20, 20 to <30, 30+, missing), body mass index in kg/m$^2$ (<25.0, 25.0 to <30.0, 30.0+, missing), smoking (never, past, current, missing), tubal ligation (yes, no, missing), and parity (0, 1 to 2, 3 to 4, 5+, children missing).

† Includes borderline cancers.

exposure. The prospective nature of our study would eliminate the potential for recall bias. Additionally, the case-control studies tended to have a younger population than our study, which included both premenopausal and postmenopausal ovarian cancers (2,8), whereas the WHI cohort consisted only of postmenopausal ovarian cancers. Ovarian cancer that occurs prior to menopause may have a different etiology than ovarian cancer occurring afterwards.

We found similar results to that of the NHS, the only other prospective cohort, which had a similar sample size and number of ovarian cancer cases to our study. Ever use of perineal powder did not appear to be associated with ovarian cancer in the NHS (9), similar to our findings. The results of Gertig and colleagues were also null for use on the genitals and for use on sanitary napkins (9). Additionally, neither our study nor the NHS found associations with serous ovarian cancer, endometrioid, or mucinous ovarian cancers, although subgroup sample size may have reduced statistical power to test these associations. In contrast to our results, the study by Gertig and colleagues found a 40% increase in invasive serous ovarian cancer among ever powder users compared with never powder users (9).

Strengths of our study included large sample size with a substantial number of ovarian cancer cases, a prospective cohort design, good case ascertainment, and detailed information on most ovarian cancer risk factors. We also had information on duration of powder use, qualifiers not available in several earlier studies, including the previous cohort study (2,8,9).

One potential limitation of our analyses includes a lack of information regarding oophorectomy after baseline, which would result in the inclusion of some women not at risk for ovarian cancer in the analytical cohort. However, the impact was likely to be minor, as a previous study in the WHI-OS had reported the number of persons with incident bilateral oophorectomies to be less than 250 (out of more than 90 000 participants) during nearly eight years of follow-up (12). While the prospective nature of the study design eliminates recall bias, it does not eliminate potential for nondifferential misclassification of the exposure. Women still needed to recall past perineal powder use and duration and thus may have trouble recollecting specifics regarding the use of perineal powder, leading to a bias toward the null. Information regarding powder use was not collected after baseline, and there is potential for never users to begin using powder; however, this is unlikely because the women are postmenopausal, reducing need to use perineal powder on diaphragms or sanitary napkins. We also had no specific data regarding the frequency of powder use in our sample. Frequency of use, as well as duration may influence ovarian cancer risk. We may have been comparing long-term infrequent users with short-term frequent users. If we had frequency of use in addition to the duration, we could have looked at intensity of use, which may be more accurate, and shown a dose response relationship. However, Terry and colleagues did not find a dose response relationship either when taking into account frequency and duration (8).

When restricted to women without tubal ligation status, the estimates for the association between combined ever perineal powder use and ovarian cancer were not increased. While some studies have found stronger associations between powder use and ovarian cancer in women that have not undergone a tubal ligation (4), the results from our study did not support this previous finding. The pooled analysis (8) and the NHS cohort (9) also did not find evidence of stronger associations in women without tubal ligations.

While we had information on duration of use, it is unknown during which years the perineal powder was used. Talc powder had potential for asbestos contamination (13) until 1976, when the Cosmetic, Toiletry, and Fragrance Association required all cosmetic talc products to be free of asbestos (14). Therefore, those using powder prior to 1976 may have been potentially exposed to asbestos, a known carcinogen. The pooled analysis and meta-analysis also included case-control studies not within the United States

(2,8), which potentially have different regulations regarding perineal powder and earlier studies that may have been more likely to include exposure to contaminated perineal powder (2). However, risk estimates in more recent studies are similar to earlier studies (2), reducing the likelihood that confounding by asbestos is driving the findings. Additionally, assuming older women in the cohort could have been exposed longer to perineal powder with potential contamination compared with younger women, we did not see statistically significant differences in risk when stratified by age group, further suggesting asbestos contamination is not a likely explanation.

The WHI-OS queried general perineal powder use rather than talc powder use, and we had no specific information regarding the content of talc in products used, which the previous literature reviewed by IARC suggested to be the possible carcinogen of concern (2). However, the NHS cohort and most studies included within the pooled analyses asked about general perineal powder use as well (2,8,9). In summary, perineal powder use did not appear to be associated with ovarian cancer risk in this large sample of postmenopausal women, even with use for long durations.

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# Exhibit 2

## The Environment and Disease: Association or Causation?

by Sir Austin Bradford Hill CBE DSC FRCP(hon) FRS
(*Professor Emeritus of Medical Statistics, University of London*)

Amongst the objects of this newly-founded Section of Occupational Medicine are firstly 'to provide a means, not readily afforded elsewhere, whereby physicians and surgeons with a special knowledge of the relationship between sickness and injury and conditions of work may discuss their problems, not only with each other, but also with colleagues in other fields, by holding joint meetings with other Sections of the Society'; and, secondly, 'to make available information about the physical, chemical and psychological hazards of occupation, and in particular about those that are rare or not easily recognized'.

At this first meeting of the Section and before, with however laudable intentions, we set about instructing our colleagues in other fields, it will be proper to consider a problem fundamental to our own. How in the first place do we detect these relationships between sickness, injury and conditions of work? How do we determine what are physical, chemical and psychological hazards of occupation, and in particular those that are rare and not easily recognized?

There are, of course, instances in which we can reasonably answer these questions from the general body of medical knowledge. A particular, and perhaps extreme, physical environment cannot fail to be harmful; a particular chemical is known to be toxic to man and therefore suspect on the factory floor. Sometimes, alternatively, we may be able to consider what *might* a particular environment do to man, and then see whether such consequences are indeed to be found. But more often than not we have no such guidance, no such means of proceeding; more often than not we are dependent upon our observation and enumeration of defined events for which we then seek antecedents. In other words we see that the event B is associated with the environmental feature A, that, to take a specific example, some form of respiratory illness is associated with a dust in the environment. In what circumstances can we pass from this

*Meeting January 14 1965*

# President's Address

observed *association* to a verdict of *causation*? Upon what basis should we proceed to do so?

I have no wish, nor the skill, to embark upon a philosophical discussion of the meaning of 'causation'. The 'cause' of illness may be immediate and direct, it may be remote and indirect underlying the observed association. But with the aims of occupational, and almost synonymously preventive, medicine in mind the decisive question is whether the frequency of the undesirable event B will be influenced by a change in the environmental feature A. *How* such a change exerts that influence may call for a great deal of research. However, before deducing 'causation' and taking action we shall not invariably have to sit around awaiting the results of that research. The whole chain may have to be unravelled or a few links may suffice. It will depend upon circumstances.

Disregarding then any such problem in semantics we have this situation. Our observations reveal an association between two variables, perfectly clear-cut and beyond what we would care to attribute to the play of chance. What aspects of that association should we especially consider before deciding that the most likely interpretation of it is causation?

(1) *Strength*. First upon my list I would put the strength of the association. To take a very old example, by comparing the occupations of patients with scrotal cancer with the occupations of patients presenting with other diseases, Percival Pott could reach a correct conclusion because of the *enormous* increase of scrotal cancer in the chimney sweeps. 'Even as late as the second decade of the twentieth century', writes Richard Doll (1964), 'the mortality of chimney sweeps from scrotal cancer was some 200 times that of workers who were not specially exposed to tar or mineral oils and in the eighteenth century the relative difference is likely to have been much greater.'

To take a more modern and more general example upon which I have now reflected for over fifteen years, prospective inquiries into smoking have shown that the death rate from cancer of the lung in cigarette smokers is nine to ten times the rate in non-smokers and the rate in heavy cigarette smokers is twenty to thirty times

as great. On the other hand the death rate from coronary thrombosis in smokers is no more than twice, possibly less, the death rate in non-smokers. Though there is good evidence to support causation it is surely much easier in this case to think of some features of life that may go hand-in-hand with smoking – features that might conceivably be the real underlying cause or, at the least, an important contributor, whether it be lack of exercise, nature of diet or other factors. But to explain the pronounced excess in cancer of the lung in any other environmental terms requires some feature of life so intimately linked with cigarette smoking and with the amount of smoking that such a feature should be easily detectable. If we cannot detect it or reasonably infer a specific one, then in such circumstances I think we are reasonably entitled to reject the vague contention of the armchair critic 'you can't prove it, there *may* be such a feature'.

Certainly in this situation I would reject the argument sometimes advanced that what matters is the absolute difference between the death rates of our various groups and not the ratio of one to other. That depends upon what we want to know. If we want to know how many extra deaths from cancer of the lung will take place through smoking (i.e. presuming causation), then obviously we must use the absolute differences between the death rates – 0·07 per 1,000 per year in non-smoking doctors, 0·57 in those smoking 1–14 cigarettes daily, 1·39 for 15–24 cigarettes daily and 2·27 for 25 or more daily. But it does not follow here, or in more specifically occupational problems, that this best measure of the effect upon mortality is also the best measure in relation to ætiology. In this respect the ratios of 8, 20 and 32 to 1 are far more informative. It does not, of course, follow that the differences revealed by ratios are of any practical importance. Maybe they are, maybe they are not; but that is another point altogether.

We may recall John Snow's classic analysis of the opening weeks of the cholera epidemic of 1854 (Snow 1855). The death rate that he recorded in the customers supplied with the grossly polluted water of the Southwark and Vauxhall Company was in truth quite low – 71 deaths in each 10,000 houses. What stands out vividly is the fact that the small rate is 14 times the figure of 5 deaths per 10,000 houses supplied with the sewage-free water of the rival Lambeth Company.

In thus putting emphasis upon the strength of an association we must, nevertheless, look at the obverse of the coin. We must not be too ready to dismiss a cause-and-effect hypothesis merely on the grounds that the observed association appears to be slight. There are many occasions in medicine when this is in truth so. Relatively few persons harbouring the meningococcus fall sick of meningococcal meningitis. Relatively few persons occupationally exposed to rat's urine contract Weil's disease.

(2) *Consistency:* Next on my list of features to be specially considered I would place the *consistency* of the observed association. Has it been repeatedly observed by different persons, in different places, circumstances and times?

This requirement may be of special importance for those rare hazards singled out in the Section's terms of reference. With many alert minds at work in industry today many an environmental association may be thrown up. Some of them on the customary tests of statistical significance will appear to be unlikely to be due to chance. Nevertheless whether chance is the explanation or whether a true hazard has been revealed may sometimes be answered only by a repetition of the circumstances and the observations.

Returning to my more general example, the Advisory Committee to the Surgeon-General of the United States Public Health Service found the association of smoking with cancer of the lung in 29 retrospective and 7 prospective inquiries (US Department of Health, Education & Welfare 1964). The lesson here is that broadly the same answer has been reached in quite a wide variety of situations and techniques. In other words we can justifiably infer that the association is not due to some constant error or fallacy that permeates every inquiry. And we have indeed to be on our guard against that.

Take, for instance, an example given by Heady (1958). Patients admitted to hospital for operation for peptic ulcer are questioned about recent domestic anxieties or crises that may have precipitated the acute illness. As controls, patients admitted for operation for a simple hernia are similarly quizzed. But, as Heady points out, the two groups may not be *in pari materia*. If your wife ran off with the lodger last week you still have to take your perforated ulcer to hospital without delay. But with a hernia you might prefer to stay at home for a while – to mourn (or celebrate) the event. No number of exact repetitions would remove or necessarily reveal that fallacy.

We have, therefore, the somewhat paradoxical position that the different results of a different inquiry certainly cannot be held to refute the

original evidence; yet the same results from precisely the same form of inquiry will not invariably greatly strengthen the original evidence. I would myself put a good deal of weight upon similar results reached in quite different ways, e.g. prospectively and retrospectively.

Once again looking at the obverse of the coin there will be occasions when repetition is absent or impossible and yet we should not hesitate to draw conclusions. The experience of the nickel refiners of South Wales is an outstanding example. I quote from the Alfred Watson Memorial Lecture that I gave in 1962 to the Institute of Actuaries:

'The population at risk, workers and pensioners, numbered about one thousand. During the ten years 1929 to 1938, sixteen of them had died from cancer of the lung, eleven of them had died from cancer of the nasal sinuses. At the age specific death rates of England and Wales at that time, one might have anticipated one death from cancer of the lung (to compare with the 16), and a fraction of a death from cancer of the nose (to compare with the 11). In all other bodily sites cancer had appeared on the death certificate 11 times and one would have expected it to do so 10–11 times. There had been 67 deaths from all other causes of mortality and over the ten years' period 72 would have been expected at the national death rates. Finally division of the population at risk in relation to their jobs showed that the excess of cancer of the lung and nose had fallen wholly upon the workers employed in the chemical processes.

'More recently my colleague, Dr Richard Doll, has brought this story a stage further. In the nine years 1948 to 1956 there had been, he found, 48 deaths from cancer of the lung and 13 deaths from cancer of the nose. He assessed the numbers expected at normal rates of mortality as, respectively 10 and 0·1.

'In 1923, long before any special hazard had been recognized, certain changes in the refinery took place. No case of cancer of the nose has been observed in any man who first entered the works after that year, and in these men there has been no excess of cancer of the lung. In other words, the excess in both sites is uniquely a feature in men who entered the refinery in, roughly, the first 23 years of the present century.

'No causal agent of these neoplasms has been identified. Until recently no animal experimentation had given any clue or any support to this wholly statistical evidence. Yet I wonder if any of us would hesitate to accept it as proof of a grave industrial hazard?' (Hill 1962).

In relation to my present discussion I know of no parallel investigation. We have (or certainly had) to make up our minds on a unique event; and there is no difficulty in doing so.

(3) *Specificity:* One reason, needless to say, is the specificity of the association, the third characteristic which invariably we must consider. If, as here, the association is limited to specific workers and to particular sites and types of disease and there is no association between the work and other modes of dying, then clearly that is a strong argument in favour of causation.

We must not, however, over-emphasize the importance of the characteristic. Even in my present example there is a cause and effect relationship with two different sites of cancer – the lung and the nose. Milk as a carrier of infection and, in that sense, the cause of disease can produce such a disparate galaxy as scarlet fever, diphtheria, tuberculosis, undulant fever, sore throat, dysentery and typhoid fever. Before the discovery of the underlying factor, the bacterial origin of disease, harm would have been done by pushing too firmly the need for specificity as a necessary feature before convicting the dairy.

Coming to modern times the prospective investigations of smoking and cancer of the lung have been criticized for not showing specificity – in other words the death rate of smokers is higher than the death rate of non-smokers from many causes of death (though in fact the results of Doll & Hill, 1964, do not show that). But here surely one must return to my first characteristic, the strength of the association. If other causes of death are raised 10, 20 or even 50% in smokers whereas cancer of the lung is raised 900–1,000% we have specificity – a specificity in the magnitude of the association.

We must also keep in mind that diseases may have more than one cause. It has always been possible to acquire a cancer of the scrotum without sweeping chimneys or taking to mule-spinning in Lancashire. One-to-one relationships are not frequent. Indeed I believe that multi-causation is generally more likely than single causation though possibly if we knew all the answers we might get back to a single factor.

In short, if specificity exists we may be able to draw conclusions without hesitation; if it is not apparent, we are not thereby necessarily left sitting irresolutely on the fence.

(4) *Temporality:* My fourth characteristic is the temporal relationship of the association – which is the cart and which the horse? This is a question which might be particularly relevant with diseases of slow development. Does a particular diet lead to disease or do the early stages of the disease lead to those peculiar dietetic habits? Does a

particular occupation or occupational environment promote infection by the tubercle bacillus or are the men and women who select that kind of work more liable to contract tuberculosis whatever the environment – or, indeed, have they already contracted it? This temporal problem may not arise often but it certainly needs to be remembered, particularly with selective factors at work in industry.

(5) *Biological gradient:* Fifthly, if the association is one which can reveal a biological gradient, or dose-response curve, then we should look most carefully for such evidence. For instance, the fact that the death rate from cancer of the lung rises linearly with the number of cigarettes smoked daily, adds a very great deal to the simpler evidence that cigarette smokers have a higher death rate than non-smokers. That comparison would be weakened, though not necessarily destroyed, if it depended upon, say, a much heavier death rate in light smokers and a lower rate in heavier smokers. We should then need to envisage some much more complex relationship to satisfy the cause-and-effect hypothesis. The clear dose-response curve admits of a simple explanation and obviously puts the case in a clearer light.

The same would clearly be true of an alleged dust hazard in industry. The dustier the environment the greater the incidence of disease we would expect to see. Often the difficulty is to secure some satisfactory quantitative measure of the environment which will permit us to explore this dose-response. But we should invariably seek it.

(6) *Plausibility:* It will be helpful if the causation we suspect is biologically plausible. But this is a feature I am convinced we cannot demand. What is biologically plausible depends upon the biological knowledge of the day.

To quote again from my Alfred Watson Memorial Lecture (Hill 1962), there was

'. . . no biological knowledge to support (or to refute) Pott's observation in the 18th century of the excess of cancer in chimney sweeps. It was lack of biological knowledge in the 19th that led a prize essayist writing on the value and the fallacy of statistics to conclude, amongst other "absurd" associations, that "it could be no more ridiculous for the stranger who passed the night in the steerage of an emigrant ship to ascribe the typhus, which he there contracted, to the vermin with which bodies of the sick might be infected". And coming to nearer times, in the 20th century there was no biological knowledge to support the evidence against rubella.'

In short, the association we observe may be one new to science or medicine and we must not dismiss it too light-heartedly as just too odd. As Sherlock Holmes advised Dr Watson, 'when you have eliminated the impossible, whatever remains, *however improbable*, must be the truth.'

(7) *Coherence:* On the other hand the cause-and-effect interpretation of our data should not seriously conflict with the generally known facts of the natural history and biology of the disease – in the expression of the Advisory Committee to the Surgeon-General it should have coherence.

Thus in the discussion of lung cancer the Committee finds its association with cigarette smoking coherent with the temporal rise that has taken place in the two variables over the last generation and with the sex difference in mortality – features that might well apply in an occupational problem. The known urban/rural ratio of lung cancer mortality does not detract from coherence, nor the restriction of the effect to the lung.

Personally, I regard as greatly contributing to coherence the histopathological evidence from the bronchial epithelium of smokers and the isolation from cigarette smoke of factors carcinogenic for the skin of laboratory animals. Nevertheless, while such laboratory evidence can enormously strengthen the hypothesis and, indeed, may determine the actual causative agent, the lack of such evidence cannot nullify the epidemiological observations in man. Arsenic can undoubtedly cause cancer of the skin in man but it has never been possible to demonstrate such an effect on any other animal. In a wider field John Snow's epidemiological observations on the conveyance of cholera by the water from the Broad Street pump would have been put almost beyond dispute if Robert Koch had been then around to isolate the vibrio from the baby's nappies, the well itself and the gentleman in delicate health from Brighton. Yet the fact that Koch's work was to be awaited another thirty years did not really weaken the epidemiological case though it made it more difficult to establish against the criticisms of the day – both just and unjust.

(8) *Experiment:* Occasionally it is possible to appeal to experimental, or semi-experimental, evidence. For example, because of an observed association some preventive action is taken. Does it in fact prevent? The dust in the workshop is reduced, lubricating oils are changed, persons stop smoking cigarettes. Is the frequency of the associated events affected? Here the strongest

support for the causation hypothesis may be revealed.

(9) *Analogy:* In some circumstances it would be fair to judge by analogy. With the effects of thalidomide and rubella before us we would surely be ready to accept slighter but similar evidence with another drug or another viral disease in pregnancy.

Here then are nine different viewpoints from all of which we should study association before we cry causation. What I do not believe – and this has been suggested – is that we can usefully lay down some hard-and-fast rules of evidence that *must* be obeyed before we accept cause and effect. None of my nine viewpoints can bring indisputable evidence for or against the cause-and-effect hypothesis and none can be required as a *sine qua non*. What they can do, with greater or less strength, is to help us to make up our minds on the fundamental question – is there any other way of explaining the set of facts before us, is there any other answer equally, or more, likely than cause and effect?

*Tests of Significance*

No formal tests of significance can answer those questions. Such tests can, and should, remind us of the effects that the play of chance can create, and they will instruct us in the likely magnitude of those effects. Beyond that they contribute nothing to the 'proof' of our hypothesis.

Nearly forty years ago, amongst the studies of occupational health that I made for the Industrial Health Research Board of the Medical Research Council was one that concerned the workers in the cotton-spinning mills of Lancashire (Hill 1930). The question that I had to answer, by the use of the National Health Insurance records of that time, was this: Do the workers in the card-room of the spinning mill, who tend the machines that clean the raw cotton, have a sickness experience in any way different from that of other operatives in the same mills who are relatively unexposed to the dust and fibre that were features of the cardroom? The answer was an unqualified 'Yes'. From age 30 to age 60 the cardroom workers suffered over three times as much from respiratory causes of illness whereas from non-respiratory causes their experience was not different from that of the other workers. This pronounced difference with the respiratory causes was derived not from abnormally long periods of sickness but rather from an excessive number of repeated absences from work of the cardroom workers.

All this has rightly passed into the limbo of forgotten things. What interests me today is this: My results were set out for men and women separately and for half a dozen age groups in 36 tables. So there were plenty of sums. Yet I cannot find that anywhere I thought it necessary to use a test of significance. The evidence was so clear-cut, the differences between the groups were mainly so large, the contrast between respiratory and non-respiratory causes of illness so specific, that no formal tests could really contribute anything of value to the argument. So why use them?

Would we think or act that way today? I rather doubt it. Between the two world wars there was a strong case for emphasizing to the clinician and other research workers the importance of not overlooking the effects of the play of chance upon their data. Perhaps too often generalities were based upon two men and a laboratory dog while the treatment of choice was deduced from a difference between two bedfuls of patients and might easily have no true meaning. It was therefore a useful corrective for statisticians to stress, and to teach the need for, tests of significance merely to serve as guides to caution before drawing a conclusion, before inflating the particular to the general.

I wonder whether the pendulum has not swung too far – not only with the attentive pupils but even with the statisticians themselves. To decline to draw conclusions without standard errors can surely be just as silly? Fortunately I believe we have not yet gone so far as our friends in the USA where, I am told, some editors of journals will return an article because tests of significance have not been applied. Yet there are innumerable situations in which they are totally unnecessary – because the difference is grotesquely obvious, because it is negligible, or because, whether it be formally significant or not, it is too small to be of any practical importance. What is worse the glitter of the $t$ table diverts attention from the inadequacies of the fare. Only a tithe, and an unknown tithe, of the factory personnel volunteer for some procedure or interview, 20% of patients treated in some particular way are lost to sight, 30% of a randomly-drawn sample are never contacted. The sample may, indeed, be akin to that of the man who, according to Swift, 'had a mind to sell his house and carried a piece of brick in his pocket, which he showed as a pattern to encourage purchasers'. The writer, the editor and the reader are unmoved. The magic formulæ are there.

Of course I exaggerate. Yet too often I suspect we waste a deal of time, we grasp the shadow and

lose the substance, we weaken our capacity to interpret data and to take reasonable decisions whatever the value of P. And far too often we deduce 'no difference' from 'no significant difference'. Like fire, the $\chi^2$ test is an excellent servant and a bad master.

*The Case for Action*

Finally, in passing from association to causation I believe in 'real life' we shall have to consider what flows from that decision. On scientific grounds we should do no such thing. The evidence is there to be judged on its merits and the judgment (in that sense) should be utterly independent of what hangs upon it – or who hangs because of it. But in another and more practical sense we may surely ask what is involved in our decision. In occupational medicine our object is usually to take action. If this be operative cause and that be deleterious effect, then we shall wish to intervene to abolish or reduce death or disease.

While that is a commendable ambition it almost inevitably leads us to introduce differential standards before we convict. Thus on relatively slight evidence we might decide to restrict the use of a drug for early-morning sickness in pregnant women. If we are wrong in deducing causation from association no great harm will be done. The good lady and the pharmaceutical industry will doubtless survive.

On fair evidence we might take action on what appears to be an occupational hazard, e.g. we might change from a probably carcinogenic oil to a non-carcinogenic oil in a limited environment and without too much injustice if we are wrong. But we should need very strong evidence before we made people burn a fuel in their homes that they do not like or stop smoking the cigarettes and eating the fats and sugar that they do like. In asking for very strong evidence I would, however, repeat emphatically that this does not imply crossing every 't', and swords with every critic, before we act.

All scientific work is incomplete – whether it be observational or experimental. All scientific work is liable to be upset or modified by advancing knowledge. That does not confer upon us a freedom to ignore the knowledge we already have, or to postpone the action that it appears to demand at a given time.

Who knows, asked Robert Browning, but the world may end tonight? True, but on available evidence most of us make ready to commute on the 8.30 next day.

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# Exhibit 3

# The evolution of evidence hierarchies: what can Bradford Hill's 'guidelines for causation' contribute?

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*'A main cause of philosophical disease – a one-sided diet: one nourishes one's thinking with only one kind of example.'* Ludwig Wittgenstein

## Introduction: when non-RCT evidence is sufficient to conclude that the intervention caused the outcome

High quality randomized controlled trials (RCTs) (concealed allocation, relevant groups blinded and sufficiently powered, etc.) will usually provide sufficient evidence to establish that a particular treatment caused an outcome. Yet sufficiently well-conducted RCTs are rare.[1] Trials can be under-powered,[2] or unsuccessfully blinded,[3,4] and often suffer from many undetected biases. The results of most RCTs are therefore often insufficient to establish causation. At the same time, RCTs are often not required to establish causation.[5] Treatments including the Heimlich manoeuvre, cardiac defibrillation and parachutes to prevent death[6] have never been tested in RCTs, yet their effectiveness is surely strongly supported by evidence.

Evidence-grading systems that place randomized trials at the top of a hierarchy[7–13] will deliver misleading conclusions in cases where RCTs are insufficient or unnecessary. According to these hierarchies, trails of homeopathy – often generating positive results and generally of higher quality than RCTs of conventional treatments[14] – will be considered to provide strong evidence, whereas the evidence base for the Heimlich manoeuvre to unblock airways and parachutes to prevent death will be judged as less strongly supported by evidence.

Sir Austin Bradford Hill, in a widely-cited 'pre-EBM' system for appraising evidence, suggested that several relevant factors must be considered before concluding causation. We investigated and revised the Bradford Hill 'guidelines for causation', in order to refine our intuitions about whether to believe that intervention is effective. Our intention is not to debunk previous attempts to grade evidence, but rather to contribute to their natural evolution and development.

## Revising Bradford Hill's guidelines

We believe that Bradford Hill's guidelines form a useful tool as they stand. Nevertheless, they can be modified in ways that make them easier to use. For instance, some of the guidelines, such as 'specificity' can safely be omitted while others, such as 'experiment' and 'strength' can be combined; still others, such as 'biological plausibility' can benefit from a more detailed analysis. Moreover, the guidelines have an inherent structure that is unclear in the original exposition. We propose that the guidelines be organized into the following three categories:

(1) *Direct evidence* from studies (randomized or non-randomized) that a probabilistic association between intervention and outcome is causal and not spurious;
(2) *Mechanistic evidence* for the alleged causal process that connects the intervention and the outcome;
(3) *Parallel evidence* that supports the causal hypothesis suggested in a study, with related studies that have similar results.

A previous attempt to impose a structure on the guidelines[15] may have oversimplified, claiming, for example, that 'analogy' (our 'similarity') is a 'mechanistic' consideration (which, as shall become clear below, is a category error).

guideline. He was also responsible for the suggestion to combine and omit some of the guidelines

**Acknowledgements**

We are grateful to Nancy Cartwright for providing useful insights during conversations with the authors. Members of the GRADE working group, especially Roman Jaeschke and Joseph Watine, provided useful feedback. Murray Enking read an earlier draft and suggested the example of folic acid to prevent neural tube defects

We use the term 'guidelines' over the more common 'criteria'[16–21] because Bradford Hill did not regard any of the guidelines as necessary or sufficient for establishing causation[11]: '… none of these viewpoints can bring indisptuable evidence for or against a cause-and-effect hypothesis and equally none can be required as a *sine qua non*'.[22] To cite his example, 'It will be helpful if the causation we suspect is *biologically plausible*, though this is a feature we cannot demand. What is biologically plausible depends on the biological knowledge of the day.'[22] Bradford Hill gave similar warnings about all the other guidelines (except, as we shall see, 'temporality'). Rather than 'criteria', they are best viewed as factors to be considered when assessing whether there is evidence for causation, or 'guidelines' for short.

Aware of detailed descriptions of the original guidelines,[15,23,24] we shall limit ourselves to describing our re-structured and revised version (Table 1). We shall then apply the Revised Bradford Hill Guidelines to real examples of likely causation despite lack of support from RCTs.

## Direct evidence

The first three of the revised guidelines help assess whether 'direct' evidence of a probabilistic association between two factors is causal rather than spurious.

**Table 1**
**Bradford Hill's original guidelines and proposed revisions**

| *Type of evidence* | *Revised, structured guidelines* | *Hill's original guidelines* |
|---|---|---|
| *Direct* | Size of effect not attributable to plausible confounding | Experiment |
| | Appropriate temporal and/or spatial proximity (cause precedes effect and effect occurs after a plausible interval; cause occurs at the same site as the intervention) | Strength |
| | Dose-responsiveness and reversibility | Temporality |
| *Mechanistic* | Evidence for a mechanism of action (biological, chemical, mechanical) | Biological gradient<br>Biological plausibility |
| *Parallel* | Coherence | Coherence |
| | Replicability | Consistency |
| | Similarity | Analogy |

### Size of effect not attributable to plausible confounding

*Plausible confounders* are factors which are not directly related to the experimental intervention, are unequally distributed between treatment and control groups, and are likely to determine the outcome. For instance, we might observe that depressed people who exercise recover more quickly. Is the association between exercise and more expedient recovery from depressive symptoms causal? We cannot answer this question without ruling out potential confounders. Those who take regular exercise might also (on average) get more sun, eat healthier foods or they might simply believe more strongly that their depression will go away. These other factors, rather than exercise, might cause their speedier recovery.

Different ailments and studies are at risk from different confounders, so the judgement of whether *plausible* confounders have been ruled out will depend on careful examination of each case. For ailments that are responsive to expectations (such as depression and pain) the confounding effects of expectations will have to be ruled out, which can be achieved by blinding the patients and caregivers. When the assessment of outcomes is prone to influence from observer bias (such as blood pressure), potential confounding by variable measurements has to be ruled out, perhaps by standardizing the measurement procedure and by blinding the investigators in charge of collecting the data and evaluating the outcomes.

Yet sometimes the *strength* of the association (the size of the effect) will be greater than the combined effect of plausible confounders. In these cases, although plausible confounders have not been ruled by the design of the study, the large observed effect has swamped the combined effects of any plausible confounders. For example, the observed effects of general anaesthesia are unlikely to be accountable by selection bias, placebo effects or reporting bias. Thus, the failure to test the effects of general anaesthetics in double-blind, placebo controlled trials should not count against our beliefs that they cause reversible loss of consciousness.

Since one should compare the strength of association (size of effect) with the potential degree of bias, we have combined these into a single comparative guideline to emphasize this intrinsic comparison: *is plausible confounding less than the size of effect?*

A note of caution about strong *relative* effects (but small absolute effects) must be issued. Although 'weak' causes may be as real as 'strong' causes, it takes fewer (or 'weaker') confounders to account for a small absolute effect than for a large absolute effect. We therefore must be more careful when inferring from a strong relative (but small absolute) effect that an association is causal. At the same time, in many cases strong relative effects can provide strong support for the causal hypothesis. For instance, although the increased risk for lung cancer in smokers Bradford Hill cited was extremely low (0.07 per 1000 for non-smokers, 0.57 for smokers), the death rate for lung cancer in cigarette smokers was over 9 times the rate for non-smokers and thus provided good evidence for causation.[22]

Our omission of the 'experiment' guideline should not be interpreted as a sign that any observational study will do. Observational studies must demonstrate larger effects than randomized trials since they are at risk from selection bias (because the allocation to treatment groups is neither randomized nor concealed) and performance bias (because the participants and caregivers are not blinded). Whether the effect size in a particular observational study is sufficiently large to rule out the combined effects of selection and performance bias will vary from case to case. If investigators conducting an observational study have been vigilant in attempts to reduce selection bias (through careful selection of the control groups and *post hoc* adjustments), and the outcome is objective, the observational study might not have to demonstrate a dramatic effect in order to support causation.[25–27] In most other cases, however, the effect in an observational study will have to be dramatic in order to be confident that plausible confounders have been ruled out.[5]

In fact, our guideline can be more stringent than current EBM standards of evidence. According to hierarchies of evidence, RCTs with a low risk of bias often provide sufficient evidence to support causation. We require that, in addition to being at low risk, the effect size outweighs the combined effects of any residual bias. For example, although most systematic reviews of high quality RCTs of SSRIs suggest that these drugs enjoy a statistically significant benefit over 'placebo',[28,29] the absolute benefit is modest – a recent study suggests it is 6% (2–9%).[30] Yet one often overlooked source of confounding in these studies is the identifiable side-effects of the drug. If patients identify the drugs because of the side-effects (and independently of their effects on depression), then their expectations regarding recovery might be higher than if they knew they were taking a 'mere' placebo. To rule out the possible confounding effect of expectations, 'active placebos', which imitate the side-effects of SSRIs need to be employed. A systematic review of antidepressants versus 'active' placebos found that the drug less placebo difference was substantially reduced.[31] Besides confounding expectations, systematic reviews of SSRIs (like most systematic reviews) are likely to be confounded to some degree by publication bias,[32,33] funding source bias[34] and data mining in the original studies.[35] A careful calculation of the combined effects of these plausible confounders must be made before claiming that the systematic reviews of SSRIs support the claim that the drugs cause the reduction in depressive symptoms. Such calculations have not (to our knowledge) been made, so this guideline, unlike current hierarchies, does not necessarily support the existence of (non-placebo) effects of SSRIs.

## Appropriate temporal and spatial proximity (encompassing and extending Bradford Hill's 'Temporality')

'Does a particular diet lead to disease or do the early stages of the disease lead to particular dietetic habits?'[22] The temporal part of this guideline is necessary: causes precede their effects and is therefore a true criterion. However, we should also ask: is the time *interval* between cause and effect consistent with the supposed mechanism? In general, the shorter the temporal and spatial interval, the less room for confounders (especially spontaneous remission) to interfere. It is equally important, for the time interval between administration of the treatment and cure to agree with the supposed mechanism of the treatment.

In some cases the *spatial* proximity between the site of administration and the outcome (see the oral

ulceration example below) may support causality – for example, thrombophlebitis at the site of injection of a cytotoxic drug. Again, the outcome need not be close to where the intervention was administered in order for the relationship to be causal, but spatial proximity generally leaves less room for confounders to interfere.

### Dose responsiveness (Bradford Hill's 'Biological gradient')

Does the outcome change when the intensity of the intervention is altered (at least if the purported mechanism predicts such a relationship)? While the presence of a dose-response relationship does not always support causality (this guideline will not be applicable for 'all or none' causes), its absence *when expected* would lead us to doubt causality. Strongest 'dose-response' evidence comes when the process is reversible. For example, the risk of lung cancer is increased in smokers but is also reduced by a half in those who stop smoking at the age of 50 years and almost completely abolished in those who stop at the age of 30.[36]

## Mechanistic evidence

Direct evidence does not always tell us *how* the intervention caused the outcome and this makes the result difficult to generalize.[37] What happens in between the intervention and the outcome is, as far as this category is concerned, a 'black box' (Figure 1). For example, Doll and Hill's famous study of the relation between the number of cigarettes smoked and the incidence of lung cancer[38] did not refer in any way to what happens between inhalation of cigarette smoke and the development of tumours in the lung. This brings us to the second category of guidelines.

Mechanisms play several roles. First, we tend to feel more confident about a treatment if the mechanism can be explained. Moreover, understanding the mechanism guides our generalization of a tightly controlled study to a wider population. Also, evidence about mechanisms plays a major role in generating hypotheses that should be tested by 'direct' tests. However, these roles of mechanism must be clearly distinguished from its distinct potential role in *confirming* hypotheses.

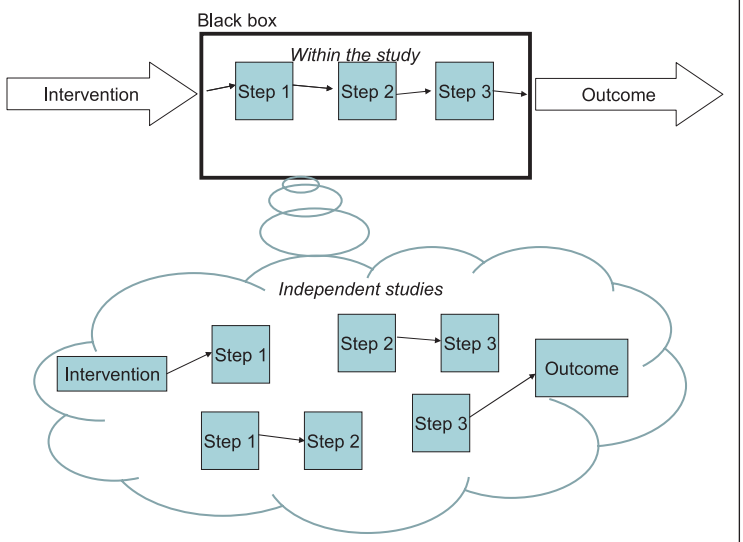
Although we believe that mechanistic evidence can provide evidential support for a causal hypothesis, two warnings are in order. Firstly, there is a difference between merely positing a mechanism (one can find a theory to explain almost anything) and providing sound evidence that there is a causal chain linking the intervention and the outcome. Secondly, appeal to mechanistic evidence has often justified the widespread use of treatments that turned out to be harmful.[40–46] Likewise, the *absence* of a plausible mechanism has often been used as a justification to ignore useful therapies such as antisepsis[47] and peptic ulceration.[48] With this in mind, although we believe that mechanistic evidence cannot be ignored, we acknowledge that mechanistic evidence should always play a subsidiary confirmatory role *vis-à-vis* direct evidence.

### Plausible mechanism

Is there evidence supporting the causal chain linking the intervention and the outcome? For example, trials testing the effect of ACE inhibitors on reduction in stroke mortality might include evidence that ACE inhibitors reduce blood pressure, that reduced blood pressure reduces the risk of stroke, and that the reduced incidence of stroke reduces mortality. Of course, each 'step' in the causal process is a new 'black box'. For example, the link between ACE inhibitors and blood pressure can be further decomposed into a series of steps, until (in a reductionist model) we bottom out at the molecular level. Bradford Hill, no doubt as an oversight, implied that plausibility was limited to 'biological plausibility'. Mechanisms of action can also be mechanical (as in the Mother's Kiss example below) or chemical (as in the oral ulceration example below).

We can envisage three 'levels' of evidential support from mechanistic evidence. Firstly, the direct study can also include studies of the causal links between the intervention and the outcome (Figure 1, top half). A second level of mechanistic evidence is when the purported mechanism of action has been demonstrated in other, independent studies (Figure 1, bottom half). For example, separate studies could establish a probable link between ACE inhibition and lower blood pressure. Obviously, having evidence for a part of the mechanism is not as strong as evidence for all the links in the causal chain.

**Figure 1**
**Direct evidence of probabilistic dependence of outcome on intervention + evidence for the causal process***




*Although Figure 1 illustrates the simple case in which the stages of the mechanism are linear, the relationship could be much more complex and include forks, cycles[39] and interactions

The second level of mechanistic evidence is closest to Bradford Hill's 'Coherence', and we have kept this guideline separate.

### Coherence

Does the causal hypothesis *cohere* with what is currently known, or is it contradicted by current knowledge? This is best explained by what happens when the evidence does not cohere. For example, the causal process by which a homeopathic remedy is purportedly effective (other than by 'placebo' effects) is not currently explicable by mainstream science. Given the numerous examples where treatments that seemed to cohere with current science that turned out to be harmful,[40–46] and where treatments that seemed *not* to cohere with current science that turned out to be helpful,[47,48] this guideline must be applied with care.

## Parallel evidence

There are rarely cases where there is only a single piece of evidence for a causal claim. When assessing whether an association is causal it is obviously necessary to consider *all* the relevant studies – this is the powerful idea underlying the importance of systematic reviews.

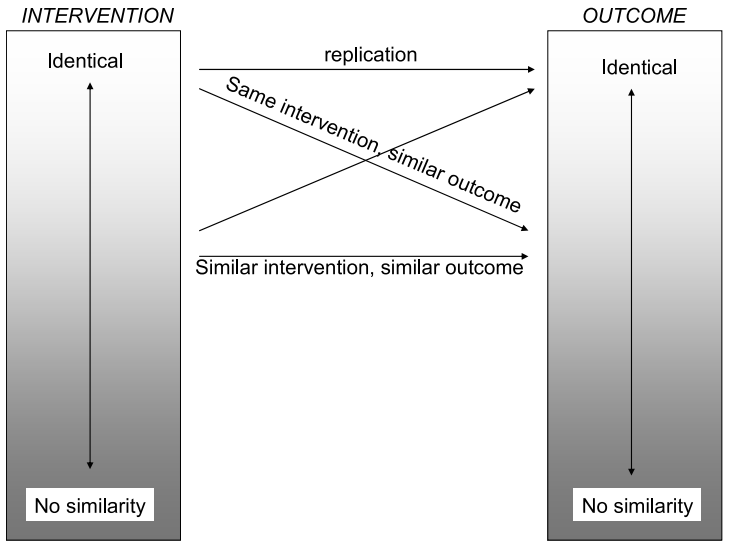
### Replicability (Bradford Hill's 'Consistency')

A study can be replicated, which means that the same intervention is tested on a similar population, using the same outcome measure. In order to count as a replication, all the elements of the study must be kept constant as far as possible. Replicability is a central tenet of scientific method: if the experiment can be repeated and provides the same results, the chances that the original results arose due to confounding is reduced. If an experiment is not replicable, either something is wrong with the attempt to replicate it or the initial experiment must be questioned.

### Similarity (of the study to other studies)

No two studies are absolutely identical, so similarities form a spectrum (Figure 2). Broadly speaking, there are several axes along which studies can differ. Firstly, the intervention can be different. If one NSAID reduced pain, we might have legitimately increased confidence that a new, similar drug would also reduce pain (although due caution would be warranted about potential adverse effects of the new drug and the benefit to harm balance). Other studies might use the same intervention and change the circumstances in which the intervention is administered. For example, we could test the intervention in a different (older or younger) population, conduct animal or *in vitro* experiments. We could also change the (geographical or socioeconomic) setting, or even the study type. Then, studies could use the same intervention but measure the outcome in different ways. If all the parallel studies gave similar results, then the causal hypothesis will be more strongly supported; if they don't, then we will have grounds to suspect either some of the parallel studies or the causal hypothesis itself. Of course, each piece of parallel evidence must be independently evaluated for validity (whether it satisfies the requirements inherent in our revised guidelines).

**Figure 2**
**Types of similarities (the axis of 'similarity of circumstances' is omitted for simplicity)**




### Omitted guidelines

Besides *experiment*, which was absorbed in our first revised guideline, we also omitted *specificity*. Diseases usually have multiple causes and multiple effects, while most interventions also have multiple effects. In fact, Bradford Hill did not support this guideline with adequate examples, and in his description of multiple regression he admits that most diseases have multiple causes and that most causes have multiple effects.[22] For example, the fact that smoking increases the risk of lung cancer in no way repudiates evidence that smoking causes other diseases. Similarly, the fact that Prozac might have a positive effect on depression does not reduce the force of the claim that it also cures premature ejaculation.

## Tests of whether the Revised Bradford Hill guidelines deliver the verdict of strong evidence for causation, even if RCTs have not been conducted

A strict application of the EBM evidence hierarchy would deliver the verdict that the following treatments are supported by relatively *poor* evidence since they have not been tested in randomized trials. After describing the examples, we shall evaluate whether the Revised Bradford Hill guidelines deliver a more reasonable verdict.

### The Mother's Kiss

Glasziou *et al.*[5] cite the following example:

> *A child presented with a plastic bead lodged high in one nostril. The doctor asked for forceps, but the nurse suggested trying the mother's kiss technique – occluding the unblocked nostril while the mother blows into the child's mouth. The bead was thus easily dislodged and retrieved.*[5]

Most would agree that a single case (or at most a series of a few cases) would suffice to support claims that the mother's kiss caused the bead to dislodge.

### Oral ulceration due to topical aspirin

Aronson and Hauben[49] have described several categories of adverse events related to drug administration that seem to require little more than anecdotal evidence to provide sufficiently strong evidence that the events are caused by adverse drug reactions. One of the categories is 'specific anatomical location or pattern of injury', in which:

> *… the location or pattern of injury is sufficiently specific to attribute the effect to the drug without the need for implicit judgment or formal investigation. The mechanism of injury can be related to physicochemical or pharmacological properties of the drug. Examples include extravasation reactions to cytostatic drugs and oral ulceration due to topical aspirin.*[49]

Here, anecdotal observations provide strong evidence that a particular drug caused an adverse event.

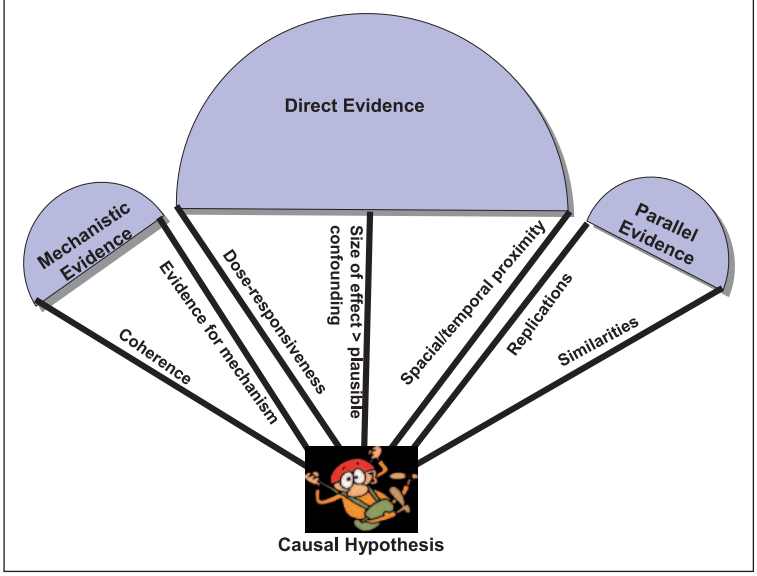
The Revised Bradford Hill guidelines deliver clear verdicts about the effectiveness of the Mother's Kiss and oral ulceration due to topical aspirin (Table 2). Admittedly the examples we chose are uncontroversial, but that is precisely why we chose them. Since nobody denies that these interventions caused their effects, while current hierarchies would deliver a poor 'grade' to their evidence base, it suggests that the Revised

**Table 2**
**Applying the Revised Bradford Hill guidelines**

| | | *Mother's kiss* | *Oral ulceration* |
|---|---|---|---|
| *Direct* | 1. Size of effect not attributable to plausible confounding | Yes (dramatic effect; confounders highly unlikely) | Yes (dramatic effect; confounders highly unlikely) |
| | 2. Appropriate temporal and/or spatial proximity | Yes (cure immediately follows the intervention and is spatially associated) | Yes (the effect is in immediate proximity to the intervention) |
| | 3. Dose-responsiveness and reversibility | Not tested and not relevant (might have been tested by varying levels of expiratory force) | Not tested (dose-responsiveness not tested; but subsequent healing suggested reversibility) |
| *Mechanistic* | 4. Plausible mechanism of action | Yes | Yes (acidic compound) |
| | 5. Coherence | Yes (nothing contradicts the causal hypothesis) | Yes (nothing contradicts the causal hypothesis) |
| *Parallel* | 6. Replicability | Yes | Not tested |
| | 7. Similarity | Not relevant | Yes (aspirin causes gastric erosions) |
| Total | | 5 'yes' *(1, 2, 4, 5, 6)* 2 'not relevant' or 'not tested' *(3,7)* | 5 'yes' *(1, 2, 4, 5, 7)* 2 'not relevant' or 'not tested' *(3, 6)* |
| *VERDICT* | | *5 out of 7 guidelines satisfied* | *5 out of 7 guidelines satisfied* |

guidelines can be useful tools for the future development and evolution of standards of medical evidence.

**Figure 3**
**How different types of evidence support the causal hypothesis**




## Conclusions: suggesting ways to revise current hierarchies of evidence

The original Bradford Hill Guidelines can be simplified (some of the guidelines can be omitted while others can be combined or modified) and organized into three categories: *direct*, *mechanistic* and *parallel* evidence. In their revised form they suggest two ways that can inform revisions to current hierarchies of evidence. Firstly, it is more important for 'direct' evidence to demonstrate that the effect size is greater than the combined influence of plausible confounders, than it is for the study to be experimental. This view is compatible with the spirit of EBM hierarchies: the motivation for placing RCTs at the pinnacle of evidence hierarchies is that they generally rule out more confounders than other study types. If an observational study reveals an effect large enough to swamp the effects of any additional confounding then other study designs must be regarded as on a par with RCTs. Likewise, RCTs must demonstrate effect sizes sufficiently large to rule out the combined effect of any inevitable bias. Secondly,

the revised guidelines illustrate how different types of evidence can complement one another (Figure 3).[50,51] Whereas a trial is often open to the objection that it is an anomaly or not generalizable, if we supplement the evidence from the trial with strong mechanistic and parallel evidence, it becomes increasingly difficult to question the results of the study and its applicability to a wider target population. A similar idea supports the use of systematic reviews, teleoanalysis[33] and the tenet of replicability in scientific method. These features of the guidelines make them particularly helpful where RCTs are unfeasible.

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# Exhibit 4

IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF NEW JERSEY

| | | |
|---|---|---|
| IN RE JOHNSON & JOHNSON TALCUM POWDER PRODUCTS MARKETING, SALES PRACTICES, AND PRODUCTS LIABILITY LITIGATION | ) | MDL NO. 16-2738 (FLW) (LHG) |
| THIS DOCUMENT RELATES TO ALL CASES | ) | |

— — —

Saturday, January 19, 2019

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Videotaped Deposition of ARCH I. "CHIP" CARSON, M.D., Ph.D., held at the Marriott Houston Medical Center, 6580 Fannin Street, Houston, Texas, commencing at 9:02 a.m., on the above date, before Michael E. Miller, Fellow of the Academy of Professional Reporters, Certified Court Reporter, Registered Diplomate Reporter, Certified Realtime Reporter and Notary Public.

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DEPOSITION EXHIBITS
ARCH I. "CHIP" CARSON, M.D., Ph.D.
January 19, 2019

DEPOSITION EXHIBITS





REFERENCED EXHIBITS



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PROCEEDINGS

(January 19, 2019 at 9:02 a.m.)

THE VIDEOGRAPHER: We are now on the record. My name is Doug Overstreet. I'm the videographer for Golkow Litigation Services. Today is January 19th, 2019. The time is 9:02 a.m.

This video deposition is being held in Houston, Texas in the matter of Talcum Powder Litigation MDL No. 2738.

The deponent is Dr. Chip Carson.

Will counsel please identify themselves for the record.

MS. O'DELL: Leigh O'Dell, Beasley Allen, for the plaintiffs.

DR. THOMPSON: Margaret Thompson, Beasley Allen, for the plaintiffs.

MS. KLEVORN: Amanda Klevorn, Burns Charest, for the plaintiffs.

MR. ZELLERS: Michael Zellers



for the Johnson & Johnson defendants.

MS. McBETH: Katherine McBeth, Drinker Biddle & Reath, for the Johnson & Johnson defendants as well.

MS. BOCKUS: Jane Bockus for Imerys.

MR. DONATH: Jonathan Donath from Coughlin Duffy for Imerys.

MS. APPEL: Renée Appel from Seyfarth Shaw for Personal Care Products.

MS. TINSLEY: Caroline Tinsley, Tucker Ellis, for PTI Union, LLC and PTI Royston, LLC.

THE VIDEOGRAPHER: The court reporter today is Mr. Mike Miller, and he will now swear in the witness.

ARCH I. "CHIP" CARSON, M.D., Ph.D., having been duly sworn, testified as follows:

EXAMINATION

BY MR. ZELLERS:

Q. Can you state your name, please.

A. Arch Carson.
Q. You are a physician; is that right?
A. I am.
Q. A medical toxicologist?
A. Yes.
Q. We are here today to take your deposition in the talc MDL litigation proceedings; is that right?
A. As far as I know, yes.
Q. You are an expert witness for the plaintiffs in that litigation; is that right?
A. Yes.
Q. Did you receive a notice of deposition, which we'll mark as Exhibit 1, to appear here today?
(Carson Deposition Exhibit 1 marked.)
A. Yes, I received a copy of this document.
MS. O'DELL: And, Michael, just for the record, we just reassert all our previously served objections to



the notice.
MR. ZELLERS: Thank you.
BY MR. ZELLERS:
Q. You have given deposition testimony in the past; is that right?
A. I have.
Q. On how many occasions?
A. Probably 30, 35.
Q. You are familiar with the procedures we're going to follow today?
A. More or less, I think.
Q. If at any time I ask you a question and you don't understand it, tell me you don't understand it and I'll repeat it or rephrase it to try to make it clear to you.
Can you do that?
A. Yes.
Q. If you answer a question that I ask or that any of the counsel ask, we're going to assume that you understood it; is that fair?
MS. O'DELL: Object to form.
A. That's fair.
///



BY MR. ZELLERS:
Q. As best we can, let me finish my question before you start to give your answer. I'll do the same and allow you to finish your answer before I ask you another question so our court reporter can take down what each of us say.
Can you do that?
A. Yes.
Q. In response to the notice of deposition, which we've marked as Exhibit 1, have you brought with you certain documents here today?
A. I have a collection of documents that in part respond to these requests, yes.
Q. Do you have any documents in your possession that are responsive to the notice of deposition, Exhibit 1, that you have not brought here today?
A. I would have to go through these things one by one, but --
Q. You didn't do that before we came here today?



A. I did, but the plaintiffs' attorneys --
MS. O'DELL: Let me just stop you, Dr. Carson, just because discussing what we've discussed is not within the purview of this deposition. That's privileged. Let me just say --
THE WITNESS: All right.
MS. O'DELL: -- Dr. Carson, in response to the notice, has brought with him copies of the cited materials in his report, and that's in the binder that is to his left.
He's brought with him copies of certain documents that were listed on his materials considered list. He doesn't have a physical copy of everything on his materials considered list.
I brought today a thumb drive that has a copy of all the items on his materials considered list. If you would like access to that, it's available to you.

And then in addition, he has brought some additional materials that he has reviewed since the service of his report.

The only other item, as I recall, on the notice of deposition request for documents that has not been brought to the deposition is copies of invoices and Dr. Carson has not sent us an invoice. That's why we don't have a copy.

So to try to short-circuit this, just to make sure since we made decisions about what's produced and what's not, I'll just say all that for the record. And if you'd like that, you're welcome to it.

BY MR. ZELLERS:

Q. Dr. Carson, you heard Ms. O'Dell describe what you brought here today. Is all of that accurate?

A. It is.

Q. Are you aware of there being any documents or materials that are



responsive to the deposition notice that you have not brought with you here today?

A. No.

Q. I'm trying to understand what counsel for plaintiffs, Ms. O'Dell, has said, so let me ask you some questions.

You have brought with you today in a binder some of the cited materials in your report; is that right?

A. Yes. This is intended to be a complete set of the cited references, with one exception.

Q. When you say cited references --

A. From my report.

Q. Your expert report, we will mark as Exhibit 2.

(Carson Deposition Exhibit 2 marked.)

BY MR. ZELLERS:

Q. Is Deposition Exhibit 2 your report in this matter?

A. It is. It also has attachments.



Q. I'll ask you about the attachments in a moment.

Does this report, Deposition Exhibit 2, contain all of the opinions that you intend to offer at any trial or hearing of this matter?

A. In general, it contains all of my opinions. I expect to expand on those opinions possibly in this deposition or in the future.

Q. Today's my opportunity to ask you what your opinions are in this matter.

As of today, are the opinions that you expressed to us set forth at any trial or hearing in this matter, are they contained in your report, Exhibit 2?

A. I have seen information that has become available recently that I did not have at that time this report was finalized, and I have modified my opinions very slightly as a result of that information.

Q. How have you modified your opinions?

A. My opinions have essentially



been strengthened as they relate to the causation question between perineal talcum powder use and the occurrence of ovarian cancers.

Q. Other than you believing that your opinions are strengthened with respect to the association between perineal talcum powder use and ovarian cancer, have your opinions changed at all since you prepared your report, Exhibit 2?

A. No.

Q. Are there any new or additional opinions as of today that you expect to testify to at trial or any hearing of this matter other than your report, Exhibit 2, and as you have qualified that report by stating that your opinions on association are stronger today?

A. No.

MS. O'DELL: Object to the form.

BY MR. ZELLERS:

Q. Okay. Your report has a list of references that begin on page 11.

Do you see that?
A. Yes.
Q. What are the references? What do they relate to? And by that, I mean -- I'm just trying to understand what this list is.
A. This is a list of references from which I gleaned information that were important to my forming opinions regarding the question that was given to me, and they contribute to pieces of the report in various ways.
They don't represent a complete review that I made in preparing my report, but all are important in some way in terms of coming to my conclusions.
Q. Are the references that you list in your report from page 11 up and through page 16, are those the materials that you are relying on in terms of your opinions that you're expressing in your report?
MS. O'DELL: Objection to form.
A. Yes.
///



BY MR. ZELLERS:
Q. What, then, is the difference between the references to your report and Exhibit B, which has a caption, Literature?
A. The Exhibit B represents a larger set of documents, including scientific literature, technical reports, and so forth that I reviewed in preparation of my report and the formation of my opinions; but they did not contain information that I felt necessary to cite in my report.
Q. The literature that you cite to as Appendix B of your report are materials that you reviewed but are not the materials that you're specifically relying on. The materials that you're specifically relying on are set forth in your references list; is that right?
MS. O'DELL: Excuse me. Object to the form, misstates his testimony.
A. My opinions are based on my total review of the literature as well as my training, my professional experience and many other factors.



I produced a report that I thought was responsive to the question that was given to me by the plaintiffs' attorneys, and within that report I felt it necessary to cite specific key references that contributed to items in that report.
BY MR. ZELLERS:
Q. And those are --
MS. O'DELL: Excuse me, sir. Are you finished, Dr. Carson?
THE WITNESS: Yes.
MS. O'DELL: Okay. Sorry.
BY MR. ZELLERS:
Q. Those are the items that you've listed under References; is that right?
A. Yes.
Q. Literature are other materials that you have reviewed but didn't rise to the level of you citing them as a reference for your report, correct?
A. That is correct, but they do contribute information that I utilize in terms of the whole to formulate my opinions.
Q. Let me mark several of the



attachments to your report as separate exhibits.
(Carson Deposition Exhibit 3 marked.)
BY MR. ZELLERS:
Q. Exhibit 3 is your curriculum vitae that was attached to your report; is that right?
A. Yes.
(Carson Deposition Exhibit 4 marked.)
BY MR. ZELLERS:
Q. Exhibit 4 is a copy of your literature list that we just discussed that is in your report; is that right?
A. Yes.
MS. O'DELL: Thank you.
BY MR. ZELLERS:
Q. The one difference with Exhibit 4, your literature list that's attached to your report as Appendix B is not numbered. I've gone ahead and numbered the pages on Exhibit 4, your literature list, in case we want to refer to a specific page.

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Today, when I refer to products, talc products, baby powder or Shower to Shower, I'm referring to the baby powder product manufactured by Johnson & Johnson Consumer Products Inc. and the Shower to Shower product formerly manufactured by Johnson & Johnson Consumer Products Inc.
Do you understand that?
A. Yes.
Q. Is your report, Exhibit 2, accurate?
A. I believe so.
Q. Do you believe it's complete?
A. In terms of its focus, yes.
Q. What do you mean in terms of its focus?
A. It covers specific aspects of a larger question, and regarding those specific aspects, I believe it is complete.
Q. It covers the aspects of the question that you intend to offer opinions on, correct?
A. That is correct.
Q. What is the question that was

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given to you by counsel for plaintiffs in this litigation?
A. The question is do the -- does the habitual use of talcum powder products cause ovarian cancer.
Q. Were you given any other questions to answer or opine on in this litigation?
A. Not specifically.
Q. What do you understand habitual use of talcum powder to refer to?
A. It means routine use, periodic use.
Q. Over any period of time?
A. Over an extended period of time.
Q. What is an extended period of time?
A. Months or years.
Q. Any other definition that you have of habitual use?
A. No.
Q. Today, in response to the notice of deposition, you did bring the

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binder of materials; is that right?
A. Yes.
Q. The binder of materials, did you prepare that, or was it prepared for you?
A. Well, I uploaded documents to a share file, and the plaintiffs' attorneys were kind enough to print those for me and assemble them in the binder.
Q. In addition, you have brought with you a stack of eight or so additional references that you have on the table in front of you; is that right?
A. Yes.
Q. Are those materials that were cited either as references in your report or in the literature section of your report?
A. I think they're all included in one or the other of those lists.
Q. Your testimony under oath is that all of the additional materials you brought here today are referred to either in your reference list, which is -- begins at page 11 of your report, or your literature list, which we've marked as Exhibit 4 and is

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Exhibit B to your report; is that right?
MS. O'DELL: Objection to the form.
Go ahead.
A. There are a couple of new articles here that were not available at the time that I submitted my report, and I believe the literature list was also created.
BY MR. ZELLERS:
Q. Were those new materials provided to you by plaintiffs' counsel or are those materials that you did some type of literature search and found?
A. One of them was provided to me by plaintiffs' counsel, but I was aware that it was coming. And -- actually, two of them were provided by plaintiffs' counsel.
Q. All right. The two additional documents that were provided to you by plaintiffs' counsel, can you show those to me?
A. Okay. One is the Longo report.
Q. We will mark as Deposition Exhibit 5 the Longo report dated

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January 15th of 2009 [sic].
(Carson Deposition Exhibit 5 marked.)
A. The other is the recent Fletcher, et al article.
(Carson Deposition Exhibit 6 marked.)
BY MR. ZELLERS:
Q. The Fletcher article dated January 3rd of 2019 we'll mark as Exhibit 6. This is an article from Reproductive Sciences; is that right?
A. Yes. And I actually have a third.
Q. All right. You have a third article that was provided to you by plaintiffs' counsel?
A. Yes.
(Carson Deposition Exhibit 7 marked.)
BY MR. ZELLERS:
Q. Let's mark that as Deposition Exhibit 7. Can you tell us what article that is?

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A. This is a meta-analysis. It's -- the title is Systematic Review and Meta-Analysis of the Association Between Perineal Use of Talc and Risk of Ovarian Cancer. The lead author is Mohamed Taher.
Q. The Taher paper we have marked as Exhibit 7; is that right?
A. Yes.
Q. This is something that you were provided by plaintiffs' counsel; is that right?
A. Yes.
Q. Exhibit 6, Reproductive Sciences, are you familiar with that journal?
A. I'm aware that it exists.
Q. Do you review that journal on a regular basis as a part of your clinical and research activities?
A. No, I don't.
Q. Is Reproductive Sciences a peer-reviewed journal?
A. I believe it is.
Q. The Exhibit 6 has as a corresponding author, Dr. Saed, S-A-E-D, a

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Ph.D.; is that right?
A. Yes.
Q. What additional articles have you brought here with you today separate and apart from your binder of materials?
A. There's a copy of the IARC monographs preamble.
Q. For what purpose did you bring that article?
A. This discusses the general process that IARC uses in approaching a putative carcinogenic material.
Q. That has previously been marked as Plaintiff Exhibit P-346 in another proceeding; is that right?
A. I don't know.
Q. Well, the document we're looking at has that exhibit sticker on it; is that right?
A. It does.
Q. What else have you brought here with you today?
A. This is an article from The Lancet from 1952 titled Value of Modified

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Starch as a Substitute for Talc, and the first author is J.D.P. Graham.
Q. Why did you bring that article?
A. This is an older article that discusses the suitability of substituting cornstarch materials for talc due to perceived issues with talc.
Q. Is this an article that you had cited previously, either in your references or your list of literature?
A. I did not cite it in my report. I don't know -- I don't recall if it's in the literature list or not.
(Carson Deposition Exhibit 8 marked.)
BY MR. ZELLERS:
Q. Why did you decide to bring that with you here today?
A. It is in the literature list. I ran across it last night, and I thought I might need to refer to it during the deposition.
Q. What other documents or materials have you brought other than your

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binder of materials?
A. I have here a copy of the recent Canadian position on the safety of talcum powder and its relationship to ovarian cancer.
Q. When did you review that document?
A. A couple weeks ago, I think.
Q. Is that a document that you were provided by plaintiffs' counsel?
A. It was.
Q. Can I see the document, please? We'll mark the draft screening assessment from Health Canada dated December 18th of 2018 as Exhibit 9.
(Carson Deposition Exhibit 9 marked.)
BY MR. ZELLERS:
Q. Any other documents?
A. I have a copy of the letter from the FDA from April 1st, 2014 responding to positions -- petitions for labeling.
Q. This is a letter that has a stamp on it on the first page, April 1st,

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2014, from -- or strike that -- to Dr. Epstein from the FDA; is that right?
A. Yes.
Q. Let's mark that as Exhibit 10.
(Carson Deposition Exhibit 10 marked.)
BY MR. ZELLERS:
Q. What else?
A. I have an article authored by A.M. Blount which is titled Amphibole Content of Cosmetic and Pharmaceutical Talcs that was published in Environmental Health Perspectives in 1991.
Q. Is that a journal that you review on a regular basis as part of either your clinical practice or your research activities?
A. That one I do look at pretty much.
Q. Is this an article you were aware of back in 1991?
A. No. At least I don't recall.
Q. Is it fair that your review of this literature, the literature relating to

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talcum powder and ovarian cancer, is something that you undertook when you were retained by plaintiffs' counsel and asked to address the question they gave to you?
A. Yes, it is.
Q. We will mark the article by Blount as Exhibit 11.
(Carson Deposition Exhibit 11 marked.)
BY MR. ZELLERS:
Q. And you have one more; is that right?
A. Yes, one more, which is -- this is an article from the American Journal of Obstetrics and Gynecology from 1974 titled The Ovarian Mesothelioma. It's authored by Parmley and Woodruff.
Q. We'll mark that as Exhibit 12.
(Carson Deposition Exhibit 12 marked.)
BY MR. ZELLERS:
Q. Exhibit 12, is this an article that was cited previously by you in either your references or your literature list?

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A. Yes.
Q. For what -- strike that.
Is this a document that you chose to bring today or were you provided it by plaintiffs' counsel?
A. This is another one I ran across last night and decided to bring along to the depo.
Q. Same questions with respect to the Blount article, Exhibit 11: Is this an article you cite in your references or literature?
A. In the literature, yes.
Q. For what purpose have you brought this with you today?
A. I thought I might want to refer to it in response to questions here.
Q. Exhibit 10, the letter from the FDA to Dr. Epstein, April of 2014, for what purpose have you brought that here with you today?
A. I thought I might want to refer to it in response to questioning.
Q. The documents that you have

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brought here with you today are documents that you wanted to have available to try to respond to the questions that I may ask you?
A. Yes.
Q. These documents you all believe -- strike that.
The documents that you've identified and you've brought with you -- have brought with you today, you believe those are supportive of the opinions that you are rendering in this matter; is that right?
A. Yes.
Q. The documents on your literature list, what we have marked as Exhibit 4, are those documents that were provided to you by plaintiffs' counsel?
A. Some were.
Q. The documents on this list that were not provided by plaintiffs' counsel, did you find those through a literature search?
A. Yes.
Q. Are you able to distinguish for us which documents on your literature list, Exhibit 4, came from plaintiffs' counsel and

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which items on the literature list you came up with?
A. To some extent.
Q. So if we went through item by item, you believe you could distinguish between what was provided to you by plaintiffs and what you found on your own?
A. For some, but not all of them.
Q. Have you reviewed all of the materials that are listed on your literature list?
A. I have reviewed all of them, yes.
Q. Have you reviewed all of the materials that are on your reference list?
A. Yes.
Q. The materials on your reference list, is it the same that some were provided to you by plaintiffs' counsel and some you found on your own?
A. I think there may be one or two references that I didn't have before I saw them in the share file that may have been provided by plaintiffs' counsel, but I

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wouldn't be able to tell you for sure. I'm sure I ran across these in my own literature search.
Q. Deposition Exhibit 13, we will mark the thumb drive that plaintiffs' counsel has brought here today.
(Carson Deposition Exhibit 13 marked.)
BY MR. ZELLERS:
Q. Do you, Dr. Carson, have an understanding of what's on the thumb drive we've marked as Exhibit 13?
A. My understanding is this is copies of the documents on the literature list.
Q. When were you first retained by anyone regarding the talc/ovarian cancer litigation?
A. In October of 2018.
Q. Who contacted you?
A. I was contacted by an attorney named Russ Abney.
Q. Who is Mr. Abney, if you know?
A. Mr. Abney is a lawyer who used

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to work in the Houston area and with whom I had some dealings years ago; and since that time he has become involved in this talc litigation in some way, was aware of me as a potential expert witness, and contacted me regarding my interest and availability.
Q. What matters have you worked on with Mr. Abney in the past?
A. I think it would have been back in the 1990s, and I frankly don't recall what cases we worked on, but there were one or maybe two cases.
Q. When in October of 2018 were you contacted by Mr. Abney?
MS. O'DELL: Object to the form.
A. I believe it was either the 14th or 15th of October.
BY MR. ZELLERS:
Q. How do you remember with that precision?
A. I have an e-mail that relates to a phone call which was our initial contact.

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Q. Mr. Abney at some point asked you to address the question that you told us before: Does the habitual use of talcum powder cause ovarian cancer?
Is that right?
MS. O'DELL: Object to the form.
A. Well, he talked to me generally about the case that was proceeding, and I discussed with him what my understanding of those things was and what the kind of opinions I would be able to render would be. And he suggested that he set up a meeting between me and members of plaintiffs' counsel.
BY MR. ZELLERS:
Q. When Mr. Abney called you middle of October of 2018, talcum powder and any relationship or association that it may have to ovarian cancer had not been a focus of your research or study; is that right?
A. That's right.
Q. It had not been a part of your clinical practice, right?

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A. That's correct.
Q. When did you meet with the larger group of plaintiffs' counsel?
A. I believe we had a telephone meeting on the 16th of October. I'm not sure. I have to --
Q. That's -- right now I just want estimates.
A. Okay.
Q. And so I don't -- as long as you're reasonably comfortable that it was in that time frame.
A. It was mid October.
Q. That's fine.
When were you asked the question that the plaintiffs' lawyers wanted you to try to answer in this litigation?
A. Well, after the meeting we parted ways and then made contact again a few days later, and I was told that they were interested in me going ahead and doing a review and starting to establish opinions.
Q. What do you mean by they authorized you or were comfortable with you

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doing a review? What does that mean?
A. Well, I felt that I was hired as a witness at that point and that's when I would begin my billable hours on this case.
Q. When was that? Sometime in later October of -- late October of 2018?
A. It was within a few days after our first meeting, still in October.
Q. What did you do to answer the question? What was your methodology?
A. Well, initially I decided to do a general literature search on the question to see what research had been performed, what reports had been written, what the quality of that research was.
Q. When did you start that?
A. Immediately. I was curious.
I began to assemble the available literature and review it on a piecemeal basis through the subsequent time period; the next couple of weeks I reviewed a lot of it.
Q. What did you search for when you did this general literature search?

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A. I searched under various search terms, including "talc," including "ovarian cancer," the relationship between the two. As I became more familiar with the literature, I expanded that search into other topics.
As I became -- I was already aware of issues related to the inclusion of asbestos in talc deposits, and so I expanded my search into that part of the literature that relates to asbestos in talc or asbestos in ovarian cancer.
As I felt my opinions would need to extend into cancer and carcinogenesis in general, I did some search into ovarian cancer specifically and general carcinogenesis to see what the current state of the art was regarding that in the literature.
I looked at some issues of mining practices.
I looked at the Johnson & Johnson website. There's a webpage regarding talc and ovarian cancer that I looked at.

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I looked through old notes and lecture files that I had for information that I've used or accessed previously in my professional capacity for information that was pertinent.

Just a very dendritic kind of extensive search.

Q. You reviewed these materials that you have told us about and then did you prepare your report?

A. At that point I -- well, the literature review took several stages. Typically when you perform a review like this, you end up with a -- I do a very general sort of approach to a review, so I get much more than will be pertinent to my review eventually.

I find that a valuable approach because it allows me to find things I wouldn't otherwise find or look for or know to look for.

And then I'm able to cull through that information and discard pieces of the search materials that are not relevant

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or interesting to me and then refine my search and redo it, extending it into different areas that have now become pertinent in my opinion, until I satisfy myself that I have pretty much covered the waterfront so to speak in terms of a literature review.

Q. You did your literature review. You reviewed the Johnson & Johnson website and the other materials that you have told us about.

Did you then formulate your opinions and set them down in your report which we marked as Exhibit 2?

A. I did. I began writing as I reviewed the literature and continued to take notes which, through a continuous editing process, eventually became my report.

Q. Did you prepare your report?

A. I did.

Q. Did anyone assist you in the preparation of your report?

A. No one assisted me in the preparation of my report. I did receive

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review of draft versions of my report and comments, in particular --

Q. Don't tell me about the comments.

A. Okay.

Q. I don't want to know what the lawyers may have told you.

Did the comments come from the lawyers for plaintiffs or did they come from other people?

A. They came from the lawyers. They also came from a few of my colleagues.

Q. Did you share your report with some of your colleagues?

A. I let a few people read it and I talked to them about it.

Q. Are the opinions your opinions?

A. Yes, they are.

Q. Have you told me, you know, generally what you have done to formulate your opinions in this matter?

A. Yes, I think so.

Q. You did all of this over a 30-day period; is that right?

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A. Yes.

Q. All right. You have no invoices, correct?

A. That's correct.

Q. Is it typical that you'll work on a matter for some number of months and not generate any invoices?

A. Yes.

Q. You are billing your time at what rate?

A. $450 per hour.

Q. Can you estimate for us the number of hours that you have spent doing your literature review, formulating your opinions, and writing your report?

A. There's still some tallying I need to do from my calendar, but it's between 150 and 180 hours.

Q. Does that include your meetings and communications with plaintiffs' counsel?

A. Yes, that's up until today.

Q. Other than meeting with Mr. Abney or talking with Mr. Abney -- did you ever meet with Mr. Abney face-to-face?

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A. No.
Q. What other plaintiff lawyers have you met with or talked with as part of your formulating your opinions and doing your literature review?
A. We've had a number of conference calls where there were several of these attorneys' colleagues on the line, but in terms of in-person meetings, those have been with Ms. O'Dell and Ms. Thompson, Dr. Thompson.
Q. How many meetings have you had with Ms. O'Dell?
A. Three.
Q. How many meetings have you had with Dr. Thompson?
A. Three.
Q. Did you know Dr. Thompson before you were retained in this matter?
A. I did not.
Q. Any other plaintiff lawyers in this litigation that you are aware of -- strike that.
Any other plaintiff lawyers in

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this matter that you've had communications with other than what you have told us?
A. No.
Q. Do you have any social relationship with any of the plaintiffs' counsel?
A. No.
Q. Your relationship with Dr. Thompson is just the three meetings that you have been involved in with her?
A. Well, we've exchanged e-mail communications, but other than that, no.
Q. Have you met with or talked with any other expert witness for plaintiffs?
A. No, I have not.
Q. Do you know who Thomas Dydek is?
A. Yes.
Q. Who is Thomas Dydek?
A. He is a toxicologist.
Q. Where does he practice?
A. I don't recall.
Q. Have you had any discussions with Dr. Dydek?

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A. I have not had any discussions with Dr. Dydek. We may have met previously, but I don't recall.
Q. Any previous meeting with Dr. Dydek, did it relate to this litigation?
A. No.
Q. Did it relate to expert witness work that you were doing?
A. No.
Q. Do you know what the relationship is, if any, between Dr. Thompson and Dr. Dydek?
A. I don't know of any relationship outside of his work as an expert witness in related litigation.
Q. Dr. Crowley, do you know Michael Crowley?
A. I know of Dr. Crowley.
Q. Did you know of Dr. Crowley before you were retained in the talcum powder litigation?
A. No.
Q. Have you ever met with Dr. Crowley?

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A. I have not.
Q. Ever talked with Dr. Crowley?
A. I have not.
Q. You reviewed his report as part of your review in this matter; is that right?
A. That's correct.
Q. Do you know who any of the other experts are in this litigation for plaintiffs?
A. Well, I know there are a number of people who have generated reports that I have also reviewed.
Q. What reports have you reviewed from plaintiffs' other experts?
A. Well, I've reviewed several reports from Dr. Longo, who's done work on the presence of asbestos in talc products and related things. I think he's the only other expert that I'm aware of at this point.
Q. Well, you're aware of Dr. Crowley?
A. Well, Dr. Crowley, Dr. Longo, and Dr. Dydek that you mentioned before.
Q. Have you reviewed any reports

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or transcripts from Dr. Dydek?
A. Yes, I reviewed an expert report that he provided before I got involved in this case.
Q. Did you review that report before you prepared your report?
A. Yes.
Q. Did you review Dr. Crowley's report before you prepared your report?
A. Yes.
Q. And you reviewed Dr. Longo's report before you prepared your report; is that right?
A. I've reviewed one report. There was another one that became available after.
Q. The second report is what you brought here with you today and we marked as Exhibit 5; is that right?
A. Yes.
Q. Any other plaintiff experts that you're aware of?
A. Not that I can think of, no.
Q. Any other reports from

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plaintiffs' experts that you have reviewed?
A. Well, there's a -- there is an article that's been submitted for publication which I consider a piece of the scientific literature. You mentioned Dr. Saed earlier, and I know that he has a relationship with this case as well.
Q. What is his relationship with this case, Dr. Saed?
A. He's provided some work at the request of the attorneys here.
Q. Have you reviewed that work?
A. That's the subject of several articles he's published previously, he and his colleagues, as well as the additional one that I brought today.
Q. Other than the articles that you have listed on your reference and literature list and the Saed article that you brought with you today, are you aware of any other work that Dr. Saed has done in this matter?
A. No.
Q. Any other plaintiff experts

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that you're aware of?
A. No.
Q. Are you aware of any of the experts for defendants in the talcum powder litigation?
A. No.
Q. Have you reviewed any reports from any of the experts in the talcum powder litigation?
A. I have not.
Q. Have you reviewed any of the transcripts of defense experts in the talcum powder litigation?
A. I've reviewed some deposition transcripts of various witnesses.
Q. Those witnesses are all listed in either your references or your literature; is that right?
A. Yes.
Q. Did you review the entire transcripts of the witnesses that you've identified?
A. I think for the most part I would say yes.

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Q. Did you review the exhibits to those depositions?
A. Yes. If they were provided to me, I did, yes.
Q. Did you believe that it was your job to do an independent assessment as to whether or not the habitual use of talcum powder causes or can cause ovarian cancer?
MS. O'DELL: Object to the form.
A. Could you repeat the question, please.
BY MR. ZELLERS:
Q. Sure.
Plaintiffs asked you to -- strike that.
Plaintiffs' counsel asked you to answer that question; is that right?
A. Yes.
Q. You understood that they were looking to develop an association or a causal relationship between the habitual use of talcum powder and ovarian cancer, correct?
A. Yes.

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MS. O'DELL: Object to the form.
Excuse me, I'm sorry, gentlemen. Give me just one second to object if I need to.
THE WITNESS: Sure.
MS. O'DELL: Thank you.
BY MR. ZELLERS:
Q. Did you consider the literature and the sources that refuted that association or causal relationship?
A. I tried to consider all the available literature.
Q. When you wrote your report setting forth your opinions, did you set forth the sources that refuted the propositions you were making?
A. I cited several sources that on the surface might seem to refute my opinions.
Q. And you believe that is contained in your report which we marked as Exhibit 2; is that right?
A. Yes.
Q. Have you been involved in any

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other talcum powder litigation other than this talc MDL matter that Mr. Abney talked to you about?
A. No, I haven't.
Q. In the 30 to 35 occasions that you've testified in the past, have any of those been on issues relating to talcum powder and any association between talcum powder and ovarian cancer?
A. No.
Q. You are not an expert in asbestos, correct?
MS. O'DELL: Object to the form.
A. I'm an occupational medicine physician, and I have a significant amount of awareness and training regarding asbestos as it relates to occupational exposures and general environmental exposures, but I don't consider myself an asbestos expert.
BY MR. ZELLERS:
Q. What percentage of your time do you spend working as a consultant? And I'm talking about your professional time.

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A. Probably 5%.
Q. What percent of your income comes from the work that you do as a consultant?
A. Of course it varies quite a bit from moment to moment, but it would be less than 10%.
Q. Have you ever testified at trial?
A. Yes.
Q. On how many occasions?
A. Probably ten.
Q. The 30 to 35 depositions that you've given previously, those have been in the context of you providing litigation consulting services; is that right?
A. In terms of expert testimony, yes.
Q. The trial appearances that you've made, are those also in your capacity as an expert witness?
A. Yes.
Q. Have you been involved in other litigations?

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A. Yes.
Q. What other litigations have you been involved in as an expert?
A. Well, I've been asked to provide opinions and testify in a number of cases, most of which involved personal injury in the occupational setting or environmental exposures.
Q. Has the majority of your expert work in the occupational setting and for environmental exposures been on behalf of plaintiffs?
A. No, it's been split about 50/50, plaintiff and defense.
Q. Have you ever been retained in a case involving cosmetic products?
A. No.
Q. Your curriculum vitae that we marked as Exhibit 3, is it correct and up to date?
A. It was up to date at the time of submission of my report in the end of 2018.
Q. What additions need to be made

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or corrections need to be made to your CV, Exhibit 3, to bring it up to date?
A. Well, I've terminated a relationship with the University of Texas Medical Branch in Galveston where I was their -- the medical director of their Employee Health Services Clinic. I continue to be -- serve as an assistant clinical professor of preventive medicine and family medicine at that institution.
I have terminated my relationship with the Enbridge Corporation as their medical director.
The Spectra Energy entry, which is about the seventh on the list of professional activities, is also terminated as that was a company that was merged and became Enbridge.
Q. Any other corrections or updates to your curriculum vitae that we've marked as Exhibit 3?
A. No.
Q. Why are you no longer serving as medical director, Employee Health Services

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with the University of Texas?
MS. O'DELL: Objection to form.
A. That was a contract that I had through the University of Texas Houston College of Nursing that provided those services to UTMB, and UTMB decided to make a change and go with another contractor.
BY MR. ZELLERS:
Q. Why are you no longer serving as medical director for Spectra Energy Corporation and Enbridge Corporation?
A. Well, Spectra Energy no longer exists; it became Enbridge Corporation. And in October of 2018, I determined that I did not -- I no longer had sufficient time to provide that service.
Q. Your undergraduate degree was in biologic sciences with a concentration in engineering; is that right?
A. Yes.
Q. You received a Ph.D. in toxicology; is that right?
A. Yes.
Q. And then later an M.D. degree;

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is that right?
A. Yes.
Q. What percentage of your time is spent in the clinical practice of medicine?
A. Currently I see patients one-half day a week and work as a supervisor of the occupational medicine residents for additional time during the week, so clinical activities would be about probably 12 hours a week.
Q. Do you see or treat women for gynecologic cancer?
A. I do not.
Q. You have never worked for a company that manufactures cosmetic products, correct?
A. That's correct.
Q. You're not a gynecologist or an oncologist, correct?
A. That's correct.
Q. You're not a cancer biologist?
MS. O'DELL: Object to the form.
A. That's correct.

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BY MR. ZELLERS:
Q. You are not a geologist, mineralogist or microscopist?
A. That's correct.
Q. You're not an epidemiologist?
A. Well, I may be considered an epidemiologist simply by my appointment as an associate professor in the Department of Epidemiology at the School of Public Health here in Houston.
Q. Do you have any professional education in the field -- well, strike that.
Have you ever published or conducted a meta-analysis?
A. I have conducted meta-analyses. I've not published them.
Q. You did not do any type of fellowship in epidemiology, correct?
A. That's correct.
Q. You're not board certified in epidemiology; is that right?
A. I don't believe there is a board certification in epidemiology.
Q. You're not a biostatistician or

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a pulmonologist?
A. That's correct.
Q. You're not a material scientist?
A. That's correct.
Q. Nor are you a pathologist?
A. Correct.
Q. You've never been involved in any pathological exam or research relating to ovarian cancer; is that right?
MS. O'DELL: Object to the form.
A. I'm not sure exactly what you mean by your question.
BY MR. ZELLERS:
Q. Sure. Let me withdraw that.
You've never been involved in terms of the research relating to ovarian cancer, correct?
A. Not specifically, no.
Q. You've never authored any literature or publications relating to talcum powder?
A. No.

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Q. Or relating to ovarian cancer, correct?
A. No.
Q. Okay. What journals -- well, strike that.
You have never published on fragrance chemicals; is that right?
MS. O'DELL: Object to the form.
A. That's correct.
BY MR. ZELLERS:
Q. Never done any research on fragrance chemicals, correct?
A. I've done some work with fragrance chemicals and health effects that are associated with them, but I have not -- I would not classify that as research or publication.
Q. You had no opinions regarding talcum powder or any of its constituent components before getting involved in this litigation; is that right?
MS. O'DELL: Object to the form.

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A. I think I had opinions about talcum powder and its constituents, but if you could be more specific, I might be able to give you a more specific answer.
BY MR. ZELLERS:
Q. Did you ever, before getting involved in this litigation in October of 2018, do research -- strike that.
You've never published on talcum powder, correct?
A. That's correct.
Q. You have never published on the constituent components of talcum powder, correct?
A. That may not be the case. I've done work in some other minerals which have resulted in publications, for example, vermiculite, which have touched on the issues of asbestos, association with talc, association with other minerals, but never specifically regarding talc.
Q. Are those publications on your CV?
A. They are.

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Q. That we marked as Exhibit 3?
A. Yes.
Q. Okay. Have you ever communicated with the FDA regarding talcum powder?
A. I've not.
Q. Have you ever communicated with Health Canada regarding talcum powder?
A. No.
Q. When did you first start preparing your report which we've marked as Exhibit 2?
A. Well, I began a literature review immediately after talking to Mr. Abney.
Q. My question, I guess, is: When did you start writing your report?
A. Well, technically I started writing my report after I was retained by plaintiffs' counsel.
Q. Late October, early November 2018?
MS. O'DELL: Object to the form, misstates his prior testimony.

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A. In October of 2018.
BY MR. ZELLERS:
Q. Have you reviewed any of the deposition transcripts of any of the experts that have been deposed in this litigation?
A. Yes.
Q. What deposition transcripts of experts have you reviewed?
A. Oh, of experts? No, I have not reviewed -- well, I've reviewed -- I've reviewed expert depositions, but I don't know what case they were deposed in, but it relates to talcum powder and ovarian cancer issue.
Q. What expert depositions have you reviewed?
A. They're all cited in the literature exhibit.
Q. All of the deposition transcripts that you've reviewed are cited in Exhibit 4?
A. I think any of the transcripts that I review are -- reviewed are probably included in here.

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Q. Are you aware of reviewing any transcripts that you did not include in your literature statement?
A. I'm not aware, but I can't tell you as I'm sitting here right now whether all of those are included in this literature statement or not.
Q. You -- looking at page --
MS. O'DELL: I'm sorry. Go ahead.
BY MR. ZELLERS:
Q. Are there any that you believe you have reviewed that are not included in the literature statement?
A. Well, let me just see here. There are --
MS. O'DELL: I think they're at the end, Dr. Carson.
THE WITNESS: At the very end.
A. Beginning on page 27 is a list of the depositions, transcripts and reports that I've reviewed, which include some of the expert witnesses, but again, I would have to say I'm -- I'm sort of unaware of the nuts and bolts of what goes on legally in this case. I know there are multiple lawsuits, and I'm not sure which ones those -- these are pertinent to.
BY MR. ZELLERS:
Q. My question is a little different and I hope pretty simple: In addition to the depositions, transcripts and reports that you have listed on pages 27 and 28 of Exhibit 4, your literature list, are there any additional depositions or transcripts that you've reviewed?
A. Pardon me for a moment while I review this.
(Document review.)
A. No, I'm not aware that there are.
BY MR. ZELLERS:
Q. Your testimony earlier was that you have reviewed each of those depositions in their entirety; is that right?
A. Yes.
Q. You have also reviewed the exhibits to those depositions; is that right?

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A. If they were made available to me, I've looked at all those exhibits as well.
Q. On page 27 of Exhibit 4, who is Annie Yessaian?
A. On page 24?
Q. Strike that. I'm sorry. On page 27 of Exhibit 4 --
A. I see.
Q. -- at the bottom, who is Annie Yessaian?
A. I don't recall.
Q. You reviewed her entire transcript and you don't recall who she is?
A. I don't.
Q. Well, go to the next page. Who is Pat Downey?
A. I believe Pat Downey is an operative of the Imerys company.
Q. Do you know what Mr. Downey's position is?
A. It's a supervisory position regarding -- regarding quality of the talc product.

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Q. Who is John Hopkins?
A. John Hopkins is an official, I believe, of -- I'm not sure -- of Johnson & Johnson, I believe, who has some oversight of talc quality as well.
Q. Susan Nicholson, who is she?
A. I don't recall.
Q. Who is Julie Pier?
A. Julie Pier is another scientist who works for Imerys, who is responsible for testing and quality.
Q. In your clinical and academic practice, do you typically rely upon depositions of company witnesses or experts?
MS. O'DELL: Object to the form.
A. If there's pertinent information in there that leads me to other areas or helps me formulate my opinions, then yes.
BY MR. ZELLERS:
Q. In the papers and publications that you have identified in your curriculum vitae, Exhibit 3, do you ever recall citing

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to company witness deposition testimony?
A. I don't typically cite deposition testimonies in published papers.
Q. You cite to various company documents. This is on pages 29 to 30 of Exhibit 4, your list of literature; is that right?
A. Yes.
Q. Did you rely on these documents in formulating your opinions?
A. Yes.
Q. Were these documents selected for you by plaintiffs' counsel?
A. Yes, they were.
Q. Are you able to identify what each of the documents are?
MS. O'DELL: Based on the Bates number?
MR. ZELLERS: Based on the Bates numbers.
A. No, I am not. I would have to look at each individual document to refresh my memory as to what it contains.
///

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BY MR. ZELLERS:
Q. Once you looked at these documents, the Imerys documents and the documents produced by the Johnson & Johnson companies, did you ask plaintiffs' counsel for any additional documents?
A. I did not. My understanding is that most of these are reports, testing reports, and most of them are positive results regarding the presence of asbestos or fibers in the product. And I know that there were many others that may not have shown positive results that I did not look at.
Q. Did you ask the plaintiff attorneys to show you or provide you with the testing documentation that showed an absence of asbestos or asbestos fibers in the talcum powder?
A. Regarding the test results that are equivalent to these that were negative, no, I did not request those.
Q. Did you review documents relating to any fragrance chemicals that are contained in or that you believe are

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contained in the talcum powder?
A. Yes. I did review some lists and, of course, Dr. Crowley's report.
Q. Do you have any idea or understanding as to the amount or amounts of the fragrance chemicals that are contained in the talcum powder in either the Johnson & Johnson Consumer company talcum powder that's involved in this litigation?
MS. O'DELL: Object to the form.
MR. ZELLERS: Let me withdraw that.
BY MR. ZELLERS:
Q. Do you know or have any understanding as to the amounts of fragrance chemicals that are in the talcum powder?
A. I do not have the specific formulation or quantities of those substances that contributed to the products.
Q. Do --
MS. O'DELL: Excuse me.
MR. ZELLERS: Ms. O'Dell, please, I'm going to let the doctor

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finish.
MS. O'DELL: In that instance, I don't know that he was, and so if he was, my apologies.
MR. ZELLERS: It's okay.
MS. O'DELL: I've been on my best behavior today, as you know, so -- but I don't want the witness to feel as if they're being cut off, and because Dr. Carson is a very polite gentlemen, he would let you interrupt him.
MR. ZELLERS: Of course.
MS. O'DELL: And I don't think that's fair.
So, Dr. Carson, if you're finished, great. If you're not, you may continue.
A. Well, I was going to say that my opinion is that there are very small quantities of those substances that contribute to the fragrance component.
BY MR. ZELLERS:
Q. Do you know how those

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quantities of fragrance chemicals may have changed over the years?
A. My understanding is they have not changed dramatically, but there have been certain substitutions over time.
Q. Do you agree that to the extent that you have reviewed internal documents, either of Imerys or from Johnson & Johnson companies, that you have only reviewed the documents that were hand-selected by the plaintiff lawyers for you to review?
MS. O'DELL: Object to the form.
A. I agree that the only documents that I've reviewed regarding the internal products of Johnson & Johnson or Imerys are the ones that were provided by the plaintiffs' attorneys.
BY MR. ZELLERS:
Q. Do you know what percentage of the documents that have been produced in this litigation by the Johnson & Johnson companies and by Imerys you have reviewed?
A. Well, based on my general

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understanding of business practices and these types of industries, I've reviewed an extremely small percentage of those.
Q. Is it your practice in your academic work or your clinical research work to rely on internal company documents?
A. Yes, it is.
Q. Do you rely on internal company documents when you publish papers?
A. In some cases.
Q. Can you tell me in what cases or instances you have relied on internal company documents in your publications?
A. Well, for example, I did -- I was involved in some research work in conjunction with NIOSH at the O.M. Scott Company at Marysville, Ohio, where we did a -- we performed a research in the company and relied on some internal documents in terms of gauging concentrations, industrial hygiene records and so forth, in order to draw conclusions that were pertinent to those publications.
Q. Was that data or were those

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internal communications that you relied on?
A. They were both.
Q. What is the publication on your CV where you relied on those materials?
A. Well, let me see here. I think the first author -- looking back here -- the first author would be Jim Lockey.
Q. Looking at page 6?
A. It's on page 6, and the -- there are two publications there. One is Pulmonary Changes After Exposure to Vermiculite Contaminated With Fibrous Tremolite that appeared in the American Review of Respiratory Disease in 1984.
There's another publication which is a book chapter called Pulmonary Hazards From Vermiculite that appeared in a book titled Health Issues Related to Metal and Nonmetallic Mining.
Q. Do you agree that when you have been provided only a small subset of the documents of a company relating to a particular product, that those documents can potentially be misleading?

MS. O'DELL: Object to the form.
A. I don't agree that that's the case because I am capable of understanding that it's a subset of available information, and I can make a reliable determination on the pertinence of that material regardless.
BY MR. ZELLERS:
Q. Without looking at any other documents or any documents that may put the documents you were provided in context?
MS. O'DELL: Object to the form.
A. It depends on the specific case, but I would say in most cases, yes.
BY MR. ZELLERS:
Q. In this case, it was not necessary for you to look at any documents other than those specific documents the plaintiffs provided to you; is that your testimony?
MS. O'DELL: Object to the form.
A. Regarding the contribution to



my opinions, I would say, yes, it was not necessary.
BY MR. ZELLERS:
Q. Did you do any independent investigation to reach your opinions, other than the literature search and review of websites that you told us about earlier?
A. Other than just general discussion with colleagues, no.
Q. Did any of the colleagues that you spoke with provide you with any substantive support for your opinions?
A. Not that I can recall. It was mostly just helpful feedback.
Q. The colleagues that you spoke with were who?
A. Various colleagues in my department or in the School of Public Health.
Q. Who?
A. Well, Dr. George Delclos, who is a pulmonologist; Dr. Brett Perkison, who is an occupational medicine physician; Roberta Ness, who is an epidemiologist.
Q. Roberta Ness is in your



department?
A. She's in my department, yes.
Q. You understand she's a lawyer -- strike that.
You understand she's an expert for the plaintiffs in this litigation?
A. I didn't know that.
Q. Dr. Ness never told you that she was an expert witness for plaintiffs in this matter?
A. No, we didn't discuss this case. We only discussed the issue.
Q. Any other colleagues that you discussed your report and opinions with?
MS. O'DELL: Object to the form.
A. I think I shared some of my thinking with the occupational medicine residents as a group and asked them to consider certain issues in the case.
BY MR. ZELLERS:
Q. Did they contribute to your review and analysis and opinions?
A. We had an interesting



discussion, but I don't think that changed my opinions in any way.
Q. The opinions that you're expressing in this case are your opinions; is that right?
A. That's correct.
Q. Your opinions you set forth in your report beginning on page 7; is that right?
A. Let me refer to my report, if you don't mind.
MS. O'DELL: Object to the form.
A. I would say -- I would say in answer to that question that, yes, my opinions do begin on page 7 of the report.
BY MR. ZELLERS:
Q. Your first opinion set forth on page 7 is that talcum powder is immunogenic and carcinogenic; is that right?
A. Yes.
MS. O'DELL: Excuse me.
BY MR. ZELLERS:
Q. Your second opinion is that

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perineal use of talcum powder results in direct exposure to the ovaries either via inhalation or migration through the female reproductive tract, correct?
A. I would not phrase the opinion in that way, but in general, that is my opinion, yes.
Q. How would you phrase your second opinion?
A. I think my second opinion relates mostly to the direct exposure to the reproductive tract that perineal use of talcum powder produces.
Q. Are you opining as to inhalation as an exposure of talcum powder to women's ovaries?
MS. O'DELL: Object to the form.
A. Only as a secondary route of exposure.
BY MR. ZELLERS:
Q. Is it part of your opinions or do you defer to other experts on inhalation?
A. I would include that as my

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opinion.
Q. So you're testifying here today that the perineal use of talcum powder results in direct exposure to the ovaries through migration through the female reproductive tract and that inhalation also results in exposure of talcum powder to the ovaries; is that right?
A. That is correct, but my basic opinion is that perineal use of talcum powder exposes the entire reproductive tract, including the pelvic cavity. So it's a bit more extensive than your phrasing.
Q. Your third opinion is very similar to your first opinion, except that here you add that it's your opinion that the ovaries are particularly susceptible to the carcinogenicity of talcum powder because they have, in your words, "no intrinsic elimination system"; is that right?
A. That's correct.
Q. Is that something you came up with on your own, no intrinsic elimination system?

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MS. O'DELL: Object to the form.
A. It's an anatomical fact. The physiology of the reproductive system does not provide the ovaries with the kind of clearance system that, for example, the lungs would have for inhaled exposures.
BY MR. ZELLERS:
Q. The words "no intrinsic elimination system," are those your words or are those words that you've seen reported in another study or another paper?
A. I think that's a fairly generic description, that those are my words.
Q. Your fourth opinion is that you believe that the epidemiological studies on talcum powder and ovarian cancer show about a 30% increased risk; is that right?
A. Correct.
MS. O'DELL: Object to the form.
BY MR. ZELLERS:
Q. As you told us at the outset, those are all still your opinions, although

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you do believe even stronger that there is a causal association between talcum powder and ovarian cancer; is that right?
A. That's correct.
Q. Have you published on your theory that baby powder causes ovarian cancer?
A. No.
Q. Do you have plans to do that?
A. Not presently.
Q. Have you conducted any tests or experiments to confirm your theory that talc migrates to the ovaries?
MS. O'DELL: Object to the form.
A. These are conclusions that I have drawn based on published literature. I wouldn't characterize them as a theory. I think they're pretty much established fact.
BY MR. ZELLERS:
Q. I'm going to ask you about all these opinions, and so we'll go through the literature and determine -- or at least I'll ask you questions about why you think that

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some of these matters are established fact.
My question is: Did you do any tests or experiments as part of your review and analysis in this matter?
A. I did not.
Q. Did you do any tests or experiments relating to your opinion that talc causes cancer via inflammation?
A. I did not.
Q. Can you identify any article that identifies inflammation anywhere in a woman's reproductive tract that results from external genital talc application?
MS. O'DELL: Object to the form.
A. I think there are a number of published articles that allude to that relationship and draw a fairly strong conclusion that it exists.
MS. O'DELL: Mike, excuse me, and I'm sorry to interrupt. We've been going over an hour and a half. Are you at a point where we can take just a short break for...

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MR. ZELLERS: Sure, we can. Let me just ask these couple of questions, and then we'll take a break.
MS. O'DELL: Sure.
BY MR. ZELLERS:
Q. So please identify for me any articles that you have reviewed that identify inflammation anywhere in a woman's reproductive tract resulting from external genital talc application.
MS. O'DELL: Objection to form.
A. I think -- I think the research evidence that includes the epidemiology piece, which is limited to external application of talcum powder, has significant enough correspondence with the biological experimentation literature that it allows us to draw those conclusions.
BY MR. ZELLERS:
Q. I understand you've drawn some conclusions here, and I'm going to ask you about these conclusions.
But what my question is: Are

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you aware of any article that identifies inflammation in a woman's reproductive tract resulting from external genital talc application?
MS. O'DELL: Object to the form.
A. I would say that the studies which have looked at that have relied on the result of internal application to show migration. There have been studies that have shown inflammation as the result of talc, and in my opinion, external application is the same as internal application in the reproductive tract.
BY MR. ZELLERS:
Q. I don't mean to be argumentative, and I don't want to be, but can you name me an article that identifies inflammation in a woman's reproductive tract resulting from external genital talc application?
MS. O'DELL: Objection, asked and answered.
A. I can't specifically.

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MR. ZELLERS: Let's take a break.
THE VIDEOGRAPHER: We're off the record, 10:37, end of Tape 1.
(Recess taken, 10:37 a.m. to 10:55 a.m.)
THE VIDEOGRAPHER: We're on the record at 10:55, beginning of Tape 2.
BY MR. ZELLERS:
Q. Dr. Carson, two of the things that you have reviewed since authoring your report in November of 2018 that you believe support your conclusions in this matter and your opinions in this matter are the draft screening assessment from Health Canada, which we marked as Exhibit 9, and the Taher paper, which has been marked as Exhibit 7; is that right?
A. Yes.
Q. Have you looked into what other public health authorities, other than Health Canada, have had to say about talc and ovarian cancer?
A. Yes, I have.

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Q. Did you -- strike that.
Are you familiar with the Center for Disease Control in the United States?
A. Yes.
Q. Did you review the CDC and its position on any relationship between talcum powder and ovarian cancer?
A. That may have been part of my review, but I don't specifically recall now what the CDC has on that issue.
Q. CDC does not list talc or talcum powder as a risk factor for ovarian cancer, correct?
A. It's quite possible.
Q. Mayo Clinic and a number of medical centers do not list talc as a risk factor for ovarian cancer, correct?
A. That may be true.
Q. Did you consider, or are you familiar with the National Cancer Institute?
A. I am.
Q. National Cancer Institute is a leading health authority in the United

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States; is that right?
A. Yes.
Q. Particularly in the area of cancer and materials that may or may not be carcinogenic; is that right?
A. Well, the National Cancer Institute is responsible for guiding national research policies as it relates to cancers, and that's one of their considerations is substances that may be related to cancer.
Q. When you reviewed what the National Cancer Institute has determined with respect to talcum powder and whether or not it is a risk factor for ovarian cancer, what did you find?
A. The most recent publication that I viewed discounts the relationship.
Q. In fact, the National Cancer Institute has concluded that the weight of the evidence does not support an association between perineal talc exposure and increased risk of ovarian cancer; is that right?
MS. O'DELL: Are you reading a quote from the document?

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MR. ZELLERS: I'm asking the doctor a question.
MS. O'DELL: Okay.
MR. ZELLERS: So --
MS. O'DELL: That's specific language, and if you have specific language that you're reading from the report or you've taken from the report, I would just ask that you show the doctor.
MR. ZELLERS: Ms. O'Dell, I have my question. I'm asking my question. The doctor can either answer my question or not answer my question. I'm not reading from a document. I'm reading from my notes.
MS. O'DELL: I object to the form of the question. I think it's unfair.
MR. ZELLERS: Can you answer that question, Doctor?
A. I would agree that that restates the general opinion of the NCI as published, but in order to verify the

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specific wording, I would need to look at the document.
BY MR. ZELLERS:
Q. Why would you rely on Health Canada but not these other public health organizations, including Center for Disease Control and the National Cancer Institute?
A. Well, there are a number of reasons. There are lots of public health organizations. Many of them have different interests and different approaches in the way that they address problems. For example, discussing the National Cancer Institute, its primary focus is on research and treatments regarding cancers, not necessarily causes, but it is a funder of basic research in the United States.
Health Canada is an organization whose charge is to -- is to synthesize public health-related positions based on evidence and disseminate those to public -- the public through various healthcare organizations or agencies. And

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for that reason, I think it's important to look at the different focus.

Also, the Health Canada report is a more contemporaneous report, which has been based on more recent science than has been considered either by the NCI or some of the other public health organizations.

Q. The NCI's most recent update to its publication was January of 2019; is that right?

MS. O'DELL: Object to the form.

A. It's current in terms of its publication. I don't know that it's January of '19; it may be. But it's still not based on the most recently available literature.

BY MR. ZELLERS:

Q. But Health Canada is; is that right?

A. Health Canada is based on more recent literature than the NCI position.

Q. Health Canada and its assessment is based upon the meta-analysis by Taher that we've marked as Exhibit 7; is that

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right?

A. It is.

MS. O'DELL: Object to the form.

BY MR. ZELLERS:

Q. You have reviewed that paper and you believe it supports and strengthens your opinions in this case; is that right?

A. Yes.

Q. Does the National Cancer Institute review the peer-reviewed literature as it relates to risk factors for ovarian cancer?

A. They have a number of committees that are set up for that purpose, and it is -- it's a committee approach which is handled by a committee chairperson. The National Cancer Institute itself has some oversight of that process, but they defer to the committee chairs.

Q. You understand that the Health Canada assessment is a draft; is that right?

A. Yes.

Q. You understand that it's at the

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very beginning of the public comment period, correct?

A. Yes.

Q. You agree that Health Canada can take up to two years to either take action or no action at all; is that right?

A. I don't know that to be the case, but it very well could be.

Q. How did you come to learn of the Health Canada risk assessment?

A. I believe the attorneys let me know about it.

Q. The attorneys for plaintiffs in this matter that retained you?

A. Yes.

Q. Were you involved in the Health Canada risk assessment prior to its publication?

A. No.

Q. Have you submitted any comments to Health Canada?

A. Not yet.

Q. Do you intend to submit comments to Health Canada?

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A. I might.

Q. What comments do you intend to submit to Health Canada?

A. I haven't formulated them yet.

Q. Outside of litigation, do you generally rely on draft assessments by regulatory agencies?

MS. O'DELL: Object to the form.

A. Yes.

BY MR. ZELLERS:

Q. Are you familiar with the precautionary principle?

A. I am.

Q. What is the precautionary principle?

A. The precautionary principle states that changes should take place in the face of a potential hazard until that hazard is proved not to exist. It's a general precept that's used in the EU, for example, and very different from the one that operates in this country.

Q. The principle in this country

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is that there needs to be scientific evidence in order to take action; is that right?
MS. O'DELL: Object to the form.
A. Yes, that's correct.
BY MR. ZELLERS:
Q. The precautionary principle says even before there's full or complete scientific demonstration of cause and effect, it is appropriate to take a precautionary approach; is that right?
A. That's right.
Q. The Health Canada follows -- strike that.
Health Canada follows and has adopted a precautionary approach; is that right?
A. Yes.
Q. Please review Deposition Exhibit 14.
(Carson Deposition Exhibit 14 marked.)
BY MR. ZELLERS:
Q. Deposition Exhibit 14 is the

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Health Canada Decision-Making Framework for Identifying, Assessing and Managing Health Risk.
Do you see that?
A. Yes.
Q. If you go to page 5 of Exhibit 14 --
MS. O'DELL: Feel free to take -- review the document if you're not familiar with it, Dr. Carson.
BY MR. ZELLERS:
Q. One of the underlying principles in the Health Canada decision-making framework is use a precautionary approach; is that right?
A. That's right.
Q. If we go to page 8, Health Canada defines the use of a precautionary approach, and looking at the second sentence: A precautionary approach to decision-making emphasizes the need to take timely and appropriate preventative action, even in the absence of a full scientific demonstration of cause and effect.

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Did I read that correctly?
A. You did.
Q. Is that your understanding of what a precautionary approach is?
A. Yes. In general, the precautionary principle can be restated that an ounce of prevention is worth a pound of cure.
Q. Health Canada does not require a finding of causation such as required in litigation matters in this country, the United States; is that right?
A. In order to adopt a document that has a significant effect on general public health practices, no, it does not.
Q. The Taher paper, that's another paper that you have reviewed since you published your report; is that right?
A. Which paper? I'm sorry.
Q. This is what we've marked as Exhibit 7. You brought it with you here today?
A. Okay. Yes.
Q. You've read the Taher 2018

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manuscript; is that right?
A. Yes.
Q. Where did you obtain that manuscript from?
A. This was obtained directly from one of the coauthors on this study to the plaintiffs' attorneys, who passed it along to me.
Q. So one of the coauthors on this study gave it to the plaintiffs' counsel, who then gave it to you; is that right?
A. That's correct.
Q. Who was the author of this publication, Exhibit 7, that provided the paper to plaintiffs' counsel, if you know?
A. I don't recall.
Q. But one of these authors; is that right?
A. It would -- yes.
Q. Why did you not include this paper on either your reliance list or your literature list?
A. I didn't have it at the time that those were formulated.

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Q. Did you have access to the appendices and supplemental tables that are referred to in the Taher 2018 publication which we've marked as Exhibit 7?
A. The ones that are not in this -- in this document or --
Q. Yes.
A. Those -- I have not thoroughly examined those, but I do have access to them.
Q. How do you have access to those appendices and supplemental tables?
A. They were also provided to me by plaintiffs' counsel.
Q. Has the Taher publication, which we've marked as Exhibit 7, been peer reviewed?
A. It's in the process. This is a manuscript that's just been accepted for publication, so it has gone through peer review.
Q. It has gone through peer review --
A. That's my understanding.
Q. -- and Exhibit 7 is the article

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that you believe will be published; is that right?
A. This is a -- this is a working manuscript which has gone through at least part of the peer-review process. There may be minor edits that occur to this, but this is substantially the final article.
Q. How do you know that?
A. That's the general process of submitting publications to peer-reviewed article -- journals.
Q. How do you know -- I'm sorry, did you finish?
A. I'm finished.
Q. How did you know the status of the peer-review process with respect to Exhibit 7?
A. Because it's been accepted for publication.
Q. How do you know that?
A. That, I was told by the plaintiffs' attorneys.
Q. And you've accepted that; is that right?

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A. Yes, I have.
Q. Do you know any of the authors of this paper, Exhibit 7?
A. No, I don't.
Q. Do you know the source of funding for this paper?
A. I -- I think the sources of funding are mentioned in here.
Q. Other than what's mentioned in the paper, Exhibit 7, do you have any knowledge as to the sources of funding?
A. There's a combination of sources. In part, this work is funded through the plaintiffs' attorneys.
Q. Have you communicated with any of the authors of this paper?
A. No.
Q. Do you know the credentials of any of the authors of this paper?
A. I haven't investigated that.
Q. In your epidemiological work outside of litigation, do you rely on articles that are funded at least in part by plaintiffs' counsel in litigation?

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A. If the articles represent good science, I don't really pay much attention or worry about the funding source.
Q. Do you know what conflicts of interest any of the authors have?
A. I don't know specifically. I can't recall if they're outlined in here. But the -- those are also evaluated based on the peer-review process.
Q. Do you know whether some of the authors are serving as consultants to plaintiffs' counsel in this litigation?
A. I know that -- no, I don't know that. Excuse me, I gave an incorrect answer.
Q. Sure. Correct it, please.
A. I mentioned that part of the funding for this research came from plaintiffs' counsel, and I'm not -- I don't know that that's the case. I was thinking of another research report when I said that.
Q. Do you know whether or not, at least in part, funding for this paper, the Taher paper, came from plaintiffs' counsel?
A. No, I don't.

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Q. Taher, this paper, Exhibit 7, concludes that asbestos contamination does not explain ovarian cancer, correct?
A. It does come to that general conclusion.
Q. That's a different conclusion than you have formulated in this matter; is that right?
A. No, it's not.
Q. You agree that asbestos contamination does not explain ovarian cancer; is that right?
A. It doesn't completely explain ovarian cancer.
Q. Does it explain ovarian cancer?
MS. O'DELL: Objection, asked and answered.
A. I -- I don't believe it completely explains ovarian cancer, no.
BY MR. ZELLERS:
Q. Turn to page 41 of Exhibit 7. Look at the last three lines of the paper. The authors of the Taher publication state: The similarity of findings between studies

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published prior to and after this point suggest asbestos contamination does not explain the positive association between perineal use of talc powder and the risk of ovarian cancer.
Did I correctly state their conclusion?
A. Well, there was a final clause of the sentence, but yes, you correctly read that.
Q. The Taher authors also discussed the lack of consistency among the various talcum powder studies; is that right?
MS. O'DELL: Object to the form.
A. I'm sorry, could you repeat that question?
BY MR. ZELLERS:
Q. Sure.
You looked at the Bradford Hill factors in formulating your opinion; is that right?
A. Yes.
Q. One of the Bradford Hill

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factors is consistency; is that right?
A. Yes.
Q. You, in fact, are opining in this case that there is consistency among the talcum powder ovarian cancer studies and publications; is that right?
A. Yes.
Q. The authors of the Taher paper disagree with that conclusion; is that right?
MS. O'DELL: Object to the form.
A. I don't think they disagree with that.
BY MR. ZELLERS:
Q. Turn to page 25, Table 2. This is, again, something that you have reviewed in preparation for your deposition; is that right?
A. Well, I didn't review it in preparation for the deposition, but I've reviewed it recently.
Q. At the request of plaintiffs' counsel, correct?
A. Yes.

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Q. Table 2 is a summary of evidence for each of the Hill criteria of causation as applied to perineal application of talc and ovarian cancer.
Do you see that?
A. Yes.
Q. Under Consistency, they state that 15 out of 30 studies reported positive and significant associations; is that right?
A. Yes.
Q. 15 out of 30, that's 50%, right?
A. Yes.
Q. 50% is no better than a coin toss; is that right?
MS. O'DELL: Object to the form.
A. Well, I would have to also mention that the majority of those 30 studies found positive associations. These are the ones that showed positive associations that rose to the level of statistical significance.
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BY MR. ZELLERS:
Q. If an association is not statistically significant, then it can be due to chance; is that right?
A. But if it's due to chance over and over and over again, and you keep getting a positive association, that argues very strongly against the chance as being the only factor.
Q. Can you answer my question: A lack of a statistically significant association is consistent with or can be consistent with no risk, correct?
MS. O'DELL: Objection to form, asked and answered.
A. If you're referring to an individual study, that might be the case; however, when considering the Bradford Hill criterion of consistency, you look at the overall body of the literature and what it tells you.
There's an obvious statistical trend toward positive connection between talcum powder perineal application and the

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occurrence of ovarian cancer, and the more evidence that mounts, the more strongly that association is proven.
BY MR. ZELLERS:
Q. Would you say that 15 out of 30 means there are consistent results across studies?
A. I think I've just explained to you how I believe there are consistent results across studies.
Q. The authors of the Taher paper also conclude that they do not find a consistent dose-response in the papers that look at perineal application of talc and ovarian cancer; is that right?
MS. O'DELL: Object to the form.
A. Well, what they actually say is that about half of the epidemiological studies assess only one level of talc exposure, ever versus never. So it's not possible from those studies to establish a biological gradient.
However, there are a number of

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studies that have shown a biological gradient at -- especially in relation to some of the subtypes of ovarian cancer.
BY MR. ZELLERS:
Q. And I'm going to ask you about those questions, but right now I'm just asking you about the Taher paper.
A. Well, I'm trying to just completely answer your question.
Q. I'm asking you about the Taher paper. You understand?
A. Yes. This is all from the Taher paper that I read you.
Q. Section 3.3.1 talks about evidence from human studies. That's on page 20; is that right?
A. Yes.
Q. This section talks about whether or not there is a consistent dose-response found in those studies; is that right?
MS. O'DELL: What sentence are you pointing to?
MR. ZELLERS: I'm asking the

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doctor questions based upon his review of the paper, Ms. O'Dell.
MS. O'DELL: Okay. Feel free to review it, Doctor, if you need to.
THE WITNESS: I'm just taking a look at this section.
BY MR. ZELLERS:
Q. And if it helps you, look on page 21, lines 174 through 177.
(Document review.)
BY MR. ZELLERS:
Q. I only want to ask you about two sentences. Are you ready for me to ask you my question?
A. Just one moment, please.
Q. Sure.
(Document review.)
THE WITNESS: All right, I'm ready for your question.
BY MR. ZELLERS:
Q. The Taher paper states that many of the studies only reported on the ovarian cancer risk assessing one exposure category and that exposure response analyses

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were not done in all studies; is that right?
A. Yes.
Q. When conducted, findings from trend analyses were not consistent; is that correct?
MS. O'DELL: Object to the form.
A. Yes.
BY MR. ZELLERS:
Q. All right. With respect -- I'm done with that paper.
You discuss your opinion number 1 on page 7 of your report; is that right?
A. Yes.
Q. You first state on page 7 that you believe talcum powder is immunogenic and produces chronic inflammation in the tissues; is that right?
A. Yes.
Q. You state that other components in talcum powder, including mineral fibers, asbestos, fibrous talc, carcinogenic metals and other chemicals intensify the

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inflammatory response and stimulate cell growth and proliferation; is that right?
A. Yes.
Q. Other than asbestos, what mineral fibers in talc intensify the inflammatory response?
A. Well, the endogenous fibrous talc fibers also intensify the response.
Q. Other than asbestos and fibrous talc fibers, what mineral fibers in talc do you believe intensify the inflammatory response?
A. I'm not really able to answer that question because I don't have a specific opinion about it. I'm not a geologist.
Q. Are the other chemicals that you refer to in this section fragrance chemicals?
A. Yes.
Q. Any others?
A. None that are intentionally added.
Q. You claim, again on page 7, that talcum powder produces chronic

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inflammation in the tissues in which it sequesters; is that right?
A. Yes.
Q. Assuming for the moment that talc can reach the ovaries, is it your opinion that talc produces chronic inflammation in the ovaries and that this somehow leads to ovarian cancer?
A. It is my opinion that talc produces chronic inflammation in the epithelial tissues of the ovaries and surrounding epithelial tissues and leads to both carcinogenesis initiation and promotion.
Q. There are no reports in the literature of externally applied talc leading to inflammation, granulomas, fibrosis or adhesions anywhere along a woman's reproductive tract, correct?
MS. O'DELL: Object to the form, asked and answered.
A. Well, that's similar to the question that you asked earlier, and although I'm not aware of experimental reports that specifically jive with that condition,

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certainly there are a lot of theoretical reports that have been published.
For example, Dr. Ness' article from '99 lays out the theory of inflammation and relates that to talc exposure from perineal application.
BY MR. ZELLERS:
Q. This is your colleague, Dr. Ness; is that right?
A. Ness, and Coussens, when she was at Pittsburgh.
Q. Dr. Ness, you showed her your report and asked for her comments; is that right?
A. I didn't show her the report.
Q. Well, you talked to her about and showed her your conclusions and your opinions; is that right?
A. No, I talked to her about the paper.
Q. Her paper?
A. Yes.
Q. Did you share with her that you were going to be an expert for the plaintiffs

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in this litigation?
A. No, I didn't.
Q. Did she wonder or ask why it was that you were researching or looking into this issue?
A. She -- I think she may have, yeah.
Q. And what did you tell her?
A. I told her I had been recently asked to look into it.
Q. Did you tell her that you'd been asked to look into it by counsel for plaintiffs in the talc litigation?
A. No, I didn't.
Q. And that never came up; is that right?
A. It didn't.
Q. And she never talked to you or told you about her experience and her work as counsel -- strike that, as an expert for plaintiffs; is that your testimony?
A. Yes. It was a very brief conversation.
Q. If up to 50% of all U.S. women

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have used genital talc, shouldn't there be studies which have shown inflammation, granulomas, fibrosis or adhesions in a woman's reproductive tract?
MS. O'DELL: Object to the form.
A. Well, there are studies that show those things.
BY MR. ZELLERS:
Q. Please, tell me the published studies that demonstrate inflammation, granulomas, fibrosis or adhesions in a woman's reproductive tract from externally applied talc?
A. Well, you're adding a new condition now.
Q. I'm sorry if I didn't add that before.
A. There are multiple studies that show inflammation and other inflammatory reactions in connection with the occurrence of ovarian cancer.
The piece that you're now asking for is the external application of

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talc relating to that, and to my knowledge, there are no experimental reports or case reports that can document that at the current time.
Q. Granulomas, fibrosis and adhesions do not cause ovarian cancer, correct?
MS. O'DELL: Object to the form.
A. The inflammatory process that is intimately connected with granuloma formation may well be the same process that results in mutation and promotion of ovarian cancer. So I -- I could not agree completely with your statement.
BY MR. ZELLERS:
Q. Is there a good scientific basis today to opine that granulomas, fibrosis or adhesions cause ovarian cancer?
MS. O'DELL: Object to the form.
A. No, I don't think they cause ovarian cancer.
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BY MR. ZELLERS:
Q. Would you agree that not all inflammatory conditions lead to cancer?
A. Yes.
Q. It's true that all of us experience inflammatory reactions of one sort or another, including chronic conditions, that do not lead to cancer, correct?
A. That's correct. Although there is a strong relationship between inflammatory processes and the occurrence of cancers, and some of those inflammatory diseases that you're referring to also have associations with increased rates of cancers.
MR. ZELLERS: Move to strike as nonresponsive.
BY MR. ZELLERS:
Q. Rheumatoid arthritis is an inflammatory condition; is that right?
A. Yes, it is.
Q. Does it increase the risk of ovarian cancer?
A. I think I -- it does -- it's not associated with ovarian cancer, but I

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think it may be associated with other cancers.
Q. Does -- strike that.
Is psoriasis an inflammatory condition?
A. Generally, it is.
Q. Is it associated with an increased risk of ovarian cancer?
A. Not that I'm aware.
Q. In your report you state that inflammation is a normal body process that leads to the thwarting of infection and rapid healing; is that right?
A. That's correct.
Q. If your inflammation theory is correct, why doesn't inflammation generally, such as in pelvic inflammatory disease, cause ovarian cancer?
A. It may do so.
Q. You are opining under oath here that pelvic inflammatory disease causes ovarian cancer?
A. I think there are experts who have concluded that.

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Q. What study are you relying on for that opinion or statement?
A. That's not part of the opinions that I've been asked to consider in this -- in this case.
Q. As you sit here, can you cite me a publication or a study that finds that pelvic inflammatory disease causes ovarian cancer?
MS. O'DELL: Object to the form.
A. Well, I have -- I have a list of studies that relate inflammation to ovarian cancer and other cancers.
BY MR. ZELLERS:
Q. Can you name me a study or a publication?
A. Okay. I think I have my list here.
Q. You brought other materials with you?
A. I brought this list.
Q. All right. Well, what list are you pulling out of your pocket?

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A. This is a list that I've put together of some of the studies I've considered and how they relate to things I might testify to today.
Q. Why did you not tell me about your list that you brought with you today before now?
A. Well, I'm telling you about it now.
Q. My question is why did you not, when I asked you what you brought to the deposition today, not take the list out and show us the list?
A. I didn't think of it.
Q. Okay. We'll mark your list as Deposition Exhibit 15.
(Carson Deposition Exhibit 15 marked.)
BY MR. ZELLERS:
Q. These are a number of notes, four pages of notes. Are these all your notes?
A. Yes.
Q. First page has got a section of

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articles on asbestos and ovarian cancer; is that right?
A. Yes.
Q. It also has inflammation and cancer and a number of studies; is that right?
A. Yes.
Q. Second page has got cohort, where you've listed out the four cohort studies; is that right?
A. Yes.
Q. Beneath that are the meta-analyses where you've listed those out and made some notes on those, correct?
A. Yes.
Q. The back page of the second page has got a listing of a number of the case-control studies, correct?
A. Yes. Those are duplicated on another page.
Q. The third page has got a section on migration and studies that you're looking at for that proposition, correct?
A. Correct.

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Q. Underneath that, ovarian cancer risk; is that right?
A. Yes.
Q. Underneath that, talc and other cancer; is that right?
A. Yes.
Q. And then on the last page, page 4, is a listing of the case-control studies with the odds ratios and confidence intervals; is that right?
A. For the most part, yes.
Q. All right. So looking now at your list of studies that you have prepared, which study demonstrates or supports the proposition that pelvic inflammatory disease causes ovarian cancer?
A. Looking through here, I don't have that item specifically in my notes, but I'm just using my notes to refresh my memory about the individual research report. I think the Coussens and Werb paper from 2010 talks about general mechanisms of inflammation in relation to the occurrence of ovarian cancer.

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And there's the Ness and Cottreau paper from '99.
Okada has discussed it in the 2007 paper. And there's a paper from 2001 which is Balkwill and Mantovani which discusses the relationship between talc and ovarian cancer and also discusses the relationship to other sources of inflammation.
Q. Each of those papers that you've identified you believe state that pelvic inflammatory disease is a cause of ovarian cancer, correct?
MS. O'DELL: Object to the form.
A. Well, I don't think they state that in so many words, but if you read the paper and you understand that -- what pelvic inflammatory disease is and its relationship to inflammatory processes in general, yes, that's what they're saying.
BY MR. ZELLERS:
Q. Doctor, my question to you was: Are you aware of any papers in which the

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authors conclude that pelvic inflammatory disease causes ovarian cancer? Do you believe each of the authors in the studies that you've identified, that their studies stand for that proposition?
MS. O'DELL: Object to form, asked and answered.
A. I think all of the studies that I've identified for this question do allude to that, yes.
BY MR. ZELLERS:
Q. That pelvic inflammatory disease causes ovarian cancer, correct?
A. That it is a -- it's a factor, yes.
Q. It's a cause. That's what they state in those papers, right?
MS. O'DELL: Object to the form.
BY MR. ZELLERS:
Q. That's your testimony?
MS. O'DELL: Excuse me, misstates his testimony. Object to the form.

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A. I would say it's a factor and leave it at that.
BY MR. ZELLERS:
Q. All right. Are you familiar with pleurodesis?
A. I am.
Q. Does a pleurodesis cause cancer?
A. It is not known to, although it might.
Q. Are you familiar with the study, 1979, A survey of the long-term effects of talc and kaolin pleurodesis?
A. Can tell me who the author of that was?
Q. Sure. The author is -- this is from the Research Committee of the British Thoracic Association. The members of the subcommittee were Chappell, Johnson, Charles, Wagner, Seal, Berry and Nicholson.
Are you familiar with that paper?
A. I'm not familiar with the paper. I may have looked at it in the past.

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Q. We'll take a look at it. We'll mark it as Deposition Exhibit 16.
(Carson Deposition Exhibit 16 marked.)
A. Thank you.
MS. O'DELL: Thank you.
BY MR. ZELLERS:
Q. This was a study that looked at the association between pleurodesis and lung cancer; is that right?
A. Yes.
Q. It's a study that you cite on page 1 of your literature list; is that right?
A. Okay. Yes.
Q. So you've read it; is that right?
A. I have.
Q. You've considered it; is that right?
A. Yes.
Q. They looked at 210 patients that underwent a pleurodesis with talc or kaolin 14 to 40 years before; is that right?

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A. That's correct.
Q. And they found that there was no increased incidence of lung cancer and no cases of mesothelioma; is that right?
A. That's correct.
Q. Why don't -- well, strike that.
You're aware of the studies that have looked at antiinflammatory drugs and aspirin use with respect to whether or not they're associated with -- let me withdraw that.
Are you familiar with the NSAID and aspirin use studies relating to the incidence of ovarian cancer in chronic users?
A. I'm familiar with some of those, yes.
Q. If your theory is correct that inflammation causes ovarian cancer, then you would expect that the studies of NSAIDs and aspirin use, antiinflammatory drugs that reduce inflammation, would consistently reduce the incidence of ovarian cancer, correct?
MS. O'DELL: Object to the form.
A. I think that was the hypothesis of those research reports.
BY MR. ZELLERS:
Q. And, in fact, the NSAID studies do not find a consistent causal reduction in the risk of ovarian cancer; is that right?
A. I think that's correct.
Q. In your report you also state that studies show that use of cornstarch instead of talcum powder reduces the risk of ovarian cancer; is that right?
A. Yes.
Q. If inflammation causes cancer, why would cornstarch be a superior alternative to talc?
A. The reason is that cornstarch, being a biological product, is much -- it does have a rapid clearance from the body, even when sequestered, in comparison with a mineral substance like talc.
Q. Well, in fact, cornstarch causes or increases the risk of inflammation, granulomas, fibrosis and adhesions, correct?

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A. It may, yes.
Q. Just like you claim talcum powder increases the risk of inflammation, granulomas, fibrosis and adhesions; is that right?
MS. O'DELL: Object to the form.
A. I think you are -- you're parsing terms here. That list of things were your words. I was agreeing with the relationship between talc and inflammation in ovarian epithelial tissue and the production or granulomas. I did not discuss the relationship between talc and adhesions or fibrosis. There was one other thing on your list.
BY MR. ZELLERS:
Q. Well, in fact, the FDA has banned the use of cornstarch as a powder for lubricating surgical gloves; is that right?
A. It has, but that's not the reason.
Q. Well, the reason that they banned the use of cornstarch is because it

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presented an unreasonable and substantial risk of illness or injury and that that risk cannot be corrected or eliminated by labeling, correct?

A. I don't know the specific language. It looks like you're reading from a Federal Register document.

The main reason that cornstarch has been banned as a lubricant in gloves is because of the potential for transmission of primarily respiratory problems through inhalation, mostly by co-workers, not by patients.

Q. You do agree that cornstarch has been banned by the FDA for use in surgical gloves; is that right?

A. All powdered gloves have been essentially banned from hospitals and operating rooms now.

Q. You also talk about inflammation and oxidative stress; is that right?

A. Yes.

Q. Does the presence of oxidative

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stress in a tissue indicate that cancer will develop in that tissue?

A. No.

Q. If exposure to a substance causes oxidative stress in certain tissue, does that mean exposure of all other tissues to that substance will cause oxidative stress in those tissues?

A. Not necessarily.

Q. Does the body have protective mechanisms that can limit tissue damage from oxidative stress?

A. Yes.

Q. Do all substances that cause oxidative stress also cause cancer?

A. I'm not sure the answer to that question is known.

Q. Are there any studies or publications that indicate that oxidative stress is involved in the development of ovarian cancer?

A. If I can define the term "oxidative stress," I could give you an answer to that, that question.

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Q. Why do you have to have a special definition of "oxidative stress"? I'm asking simply: Is there a publication or a study which documents that oxidative stress is involved in the development of ovarian cancer?

MS. O'DELL: Object to the form.

A. Sure.

BY MR. ZELLERS:

Q. And what paper are you going to point me to?

A. Well, I'll point you to the Ness paper to begin with, because it was one of the earlier papers that related oxidative stress from talc to the occurrence of ovarian cancer. But the relationship between inflammation, which essentially is the source of the oxidative stress, and cancer goes all the way back into the 19th Century in terms of its proposal as a rationale.

Q. Is oxidative stress a variation of inflammation as you're using that term relating to a potential cause of ovarian

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cancer?

A. It's a component of inflammation.

Q. As a toxicologist, how would you define fibrous talc?

A. Fibrous talc is a form of talc that is conformed into elongated structures that have an aspect ratio of length greater than width that is different from the majority of talc which is the platy form.

Q. Do you consider yourself to be an expert on fibrous talc?

A. No, I don't.

Q. Do you consider yourself to be an expert on oxidative stress?

A. I have dealt a lot with issues of oxidative stress and health effects resulting from it.

Q. Do you consider yourself to be an expert in oxidative stress?

MS. O'DELL: Objection, asked and answered.

A. I'm not a specific expert in oxidative stress, but I can -- I can opine

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regarding my professional understanding and training.
BY MR. ZELLERS:
Q. You've never been involved in terms of any research or publication on the subject of oxidative stress and any association with ovarian cancer, correct?
A. Not in terms of ovarian cancer, no.
Q. You have not been involved in any research or publication relating to the subject of inflammation and its association with ovarian cancer, correct?
A. No. All right. Yes, correct.
Q. Yes, it is correct? Okay.
You claim that the presence of asbestos and fibrous talc further intensifies the carcinogenic effect of talc; is that right?
A. Yes.
Q. Is that statement different from the statement directly above where you allege that asbestos and mineral fibers intensify the inflammatory response and

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stimulate the cell growth and proliferation?
A. It's not different, no.
Q. Are your opinions dependent on talc containing carcinogenic asbestos and/or fibrous talc?
A. No.
Q. Do you believe that talcum powder without asbestos causes ovarian cancer?
A. I believe talcum powder causes ovarian cancer. I have not seen any research done on talcum powder that has been shown not to contain asbestos.
Q. Your assumption that you have made in formulating your opinions here is that talcum powder contains asbestos; is that right?
A. No.
Q. What assumption have you made as to whether or not talcum powder contains either asbestos or fibrous talc?
MS. O'DELL: Object to the form.
A. Looking at the research

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reports, the epidemiology first, is looking at the relationship between perineal use of dusting powders, talcum powders and ovarian cancer.
Although there have been efforts in some of those studies to characterize the proportion or the ingredients that would be either asbestos or fibers, that's not done in all cases, and it's not ruled out in any cases.
The -- also, the research studies that have been performed, the testing, for example, of the products themselves are replete with reports of components of these powders that are fibrous in nature.
MR. ZELLERS: Move to strike as nonresponsive.
BY MR. ZELLERS:
Q. Do you believe that all talcum powder products that are on the market contain asbestos?
MS. O'DELL: Object to the form.

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A. I don't know.
BY MR. ZELLERS:
Q. Does it matter to your opinion as to whether or not the talcum powder products, and particularly the talcum powder products involved in this case, contain asbestos?
A. I wouldn't have a way to be able to answer that yes or no.
Q. Do you -- strike that.
Have you reached a conclusion as to whether or not the talcum powder products involved in this case contain fibrous talc?
A. I think that most of them do.
Q. Does all of the talcum powder contain fibrous talc or just some of it?
A. Certainly a lot of it does.
Q. The basis for your conclusion that the talcum powder at issue in this case contains fibrous talc is the testing reports that plaintiffs' attorneys gave you?
MS. O'DELL: Object to the form.

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A. Yes. Also Longo's publications and reports.
BY MR. ZELLERS:
Q. You have reviewed the Longo reports; is that right?
A. Yes.
Q. Have you ever met with him?
A. No.
Q. Do you know his qualifications?
A. I looked at his qualifications at one point, but I don't recall exactly what it is at this stage.
Q. Ever hear of him before this lawsuit, your getting involved in the talc litigation back in October of 2018?
A. No.
Q. Have you reviewed any of Longo's testing where he did not find asbestos?
A. I -- the only thing I've reviewed are what's present in those reports that I cited.
Q. Were you provided by counsel for plaintiffs with any testing reports from

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Longo where he did not find asbestos?
A. There are some of those listed in his reports.
Q. Have you reviewed the FDA's testing of talcum powder products?
A. The FDA didn't really do much testing of talcum powder products.
Q. Have you reviewed the FDA's testing of talcum powder products?
MS. O'DELL: Objection, vague.
A. The only FDA testing that I looked at was the -- I have it referenced in my list, but the FDA, based on a recommendation, requested samples from various companies, I think nine different sources of talc. They received four and tested those. And based on their test method determined that there was not a -- not evidence of a significant hazard.
BY MR. ZELLERS:
Q. Have you made any effort to quantify the amount of any alleged contaminant in the Johnson & Johnson Consumer talcum powder?

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MS. O'DELL: Object to the form.
A. That wasn't my charge. I defer to the other experts in this case.
BY MR. ZELLERS:
Q. Do you have an opinion on what type of asbestos you believe is in the talcum powder products at issue in this case?
A. Well, there have been various types shown, but I think for the most part it's tremolite and anthophyllite.
Q. Are you familiar with crocidolite?
A. Yes.
Q. Is crocidolite found in talcum powder or baby powder?
A. It's not commonly found in it.
Q. You believe that the asbestos -- types of asbestos that may be in the talcum powder at issue in this case is tremolite and acidolite [sic]?
MS. O'DELL: Objection.
A. Anthophyllite. There are others found, but you asked for most common.

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BY MR. ZELLERS:
Q. Most common you believe are tremolite and anthophyllite?
A. Anthophyllite.
Q. Anthophyllite. Those two; is that right?
A. Yes.
Q. What types of asbestos are associated with ovarian cancer?
A. Well, I'll go back to my list again. Crocidolite is associated with ovarian cancer in the Acheson report from 1982, which was from female gas mask manufacturers in England who made gas masks during the period of the Second World War, and crocidolite is associated with that with a fairly high relative risk of 2.96. Chrysotile asbestos had also a positive relative risk of 1.74.
There was a study of factory workers and pipe laggers in east London, which is the Berry report from 2000, that showed a relative risk of 2.53, and those workers were exposed to primarily asbestos

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cement products and plasters, so the --
Q. What type of asbestos, if you know?
A. That would have been primarily amphibole asbestos types, which would include crocidolite and tremolite and anthophyllite, amosite is in that category.
Bertolotti in 2008 published a report -- actually, there were several reports that resulted from the Eternit factory studies in Casale Monferrato in Italy, which was a plant that manufactured cement sheet and corrugated tubing, and there were a number of studies that showed elevated relative risks in persons exposed to asbestos in that work, and that would also have been amphibole asbestos types.
Q. The studies that you've recited for us, those are all occupational studies; is that right?
A. Yes. I've got a lot more.
Q. Well, and it's on your list, which we marked as Exhibit 15; is that right?
A. That's correct.

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Q. All right. Those studies did not involve the perineal application of talcum powder products; is that right?
MS. O'DELL: Object to the form.
A. It was not a factor in the study.
BY MR. ZELLERS:
Q. Crocidolite and chrysotile asbestos has generally not been found in talcum powder products, correct?
A. In general, that's the case.
Q. Was there ever a point in time where you believe that the talcum powder products involved in this case were not contaminated with asbestos?
MS. O'DELL: Objection to form, vague as to time.
A. My understanding is that Imerys and their predecessors and Johnson & Johnson made significant efforts to reduce components of asbestos in their talc products over a number of years and made step-wise progress in doing that.

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But based on my current understanding, I don't believe they've ever been totally successful in doing so.
So in answer to your question, which I think was, was there ever a point in time where you believe the talcum powder products involved in this case were not contaminated with asbestos, no.
BY MR. ZELLERS:
Q. You cite in your report, page 5, to two exhibits to the depositions of John Hopkins and Julie Pier in support of your opinion that talcum powder products contain asbestos; is that right?
A. That's correct.
Q. Looking at page 5, footnote 1, you cite to Exhibit Hopkins-28 in the Hopkins deposition and Exhibit Pier-47 in the Pier deposition; is that right?
A. That's correct.
Q. Are you aware that those exhibits were created by plaintiffs' counsel?
MS. O'DELL: Objection to form.
A. I didn't -- I -- I don't know

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that and doesn't matter to me.
BY MR. ZELLERS:
Q. Do you know where the data in those exhibits come from?
A. Well, they come from the two persons who are testifying who have produced them from their -- mostly from their business records.
Q. Okay. So you believe that Exhibit Hopkins-28 to the Hopkins deposition and Exhibit Pier-47 to the Pier deposition come from the business records of the Johnson & Johnson Company and Imerys?
A. From the most part, there was a -- there was a table that was constructed during the deposition which was sort of a piece of summary information. I don't know if it's an exhibit to the deposition or if it's something separate from that, but it would not have been from business records, but occurred at the deposition itself.
MS. O'DELL: Excuse me, Dr. Carson, would you like to see a copy of exhibit -- of the Hopkins

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Exhibit Hopkins-28 and Pier Exhibit Pier-47 in answering these questions?
THE WITNESS: If that's easy to do, yes.
MS. O'DELL: It's very easy to do. This is a copy of Exhibit Hopkins-28 of the Hopkins deposition and Exhibit Pier-47 of the Pier deposition.
THE WITNESS: Okay.
BY MR. ZELLERS:
Q. Dr. Carson?
A. Yes, sir.
Q. Did you make any effort to investigate the alternative explanations for the data that's contained in those two exhibits, Exhibit Hopkins-28 and Exhibit Pier-47?
A. Alternative explanations, I'm not sure what you mean by that.
Q. If the Johnson & Johnson company -- companies' scientists and Imerys' scientists opined that those tests don't

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actually show asbestos, you have no expertise to dispute that, do you?
MS. O'DELL: Object to the form.
A. No, I don't have any personal expertise to dispute that.
BY MR. ZELLERS:
Q. Do you know whether or not any of the talc product that is identified on Exhibit Hopkins-28 and Exhibit Pier-47 was actually used in the talcum powder products that were sold by the Johnson & Johnson Consumer Products company?
MS. O'DELL: Objection to form.
A. I -- it's my understanding that some of these results, at least -- in particular from the Pier deposition, that some of these results were from testing that was done on material that had already been shipped and probably incorporated into products.
BY MR. ZELLERS:
Q. Do you know whether or not any of the talc that is referred to on the two

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exhibits you're looking at, Exhibit Hopkins-28 and Exhibit Pier-47, were included in talcum powder product sold by J&J Consumer Products?
MS. O'DELL: Objection to the form, asked and answered.
A. No, I don't.
BY MR. ZELLERS:
Q. Have you confirmed -- strike that.
What amount of asbestos exposure is associated with ovarian cancer?
A. Any.
Q. Your testimony under oath is that any asbestos exposure is associated with ovarian cancer?
A. Any asbestos exposure and any perineal application of talcum powder is associated with an increased risk for ovarian cancer.
Q. The amount of asbestos contained -- or allegedly contained within the baby powder is of no consequence, correct?

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MS. O'DELL: Object to the form.
A. No, it is of consequence, and a larger dose would be a greater hazard. But that doesn't mean that a low dose is not a hazard.
BY MR. ZELLERS:
Q. My question is: Do you know the amount of alleged asbestos exposure that's associated with ovarian cancer?
A. No.
Q. Do you know the type of ovarian cancer that asbestos is associated with?
MS. O'DELL: Object to the form.
A. It's associated mostly with the collection of epithelial ovarian cancers --
BY MR. ZELLERS:
Q. What --
A. -- primarily serous.
Q. Does the type of ovarian cancer vary based upon the type of asbestos?
A. Not that I'm aware of.
Q. You believe that all types of

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asbestos can produce all types of ovarian cancer; is that correct?
MS. O'DELL: Object to the form.
A. I suspect that some forms of asbestos are much more carcinogenic than others, and that would be true for the ovaries as well as other structures in the body.
BY MR. ZELLERS:
Q. Are you able to distinguish for us what types of asbestos cause or are associated with what types of ovarian cancer?
A. I don't think I'm able to make those distinctions, but the studies I just read to you regarding the relationship between asbestos and ovarian cancer and the others on my list do indicate that there are, for example, in the Acheson study, there were -- there was a positive relationship between both crocidolite and chrysotile exposure, and the crocidolite had a greater effect on ovarian cancer than the chrysotile, but did not have -- they were both positive.

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Q. What type of ovarian cancer?
A. That, I don't know at the moment. I could look in the paper and see if it's listed.
Q. There are a number of different types of ovarian cancer; is that right?
A. That's correct.
Q. You are not familiar with J&J Consumer Products' procedures for milling or mining; is that right?
MS. O'DELL: Object to the form.
A. I'm familiar with some of their procedures, yes.
BY MR. ZELLERS:
Q. Are you familiar with their testing of source mines?
A. To some extent.
MS. O'DELL: Object to the form.
BY MR. ZELLERS:
Q. Is it set forth in your report, or is that just background information that you looked at?

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A. That's background information and my personal knowledge.
Q. You are not going to give an opinion on mines, mining or milling in this case; is that right?
A. Depends on the questions.
Q. Well, as you sit here today, do you intend to give opinions on talc mining, mines or milling?
A. It wasn't my intention, but if asked a question that I think I'm qualified to answer, I'll try to do it.
Q. Are you an expert on talc mining and milling?
A. I'm an expert on industrial processes in general, and if -- I have some personal understanding of talc mining and milling.
Q. Have you been personally involved in talc mining and milling?
A. I haven't been involved in it; I've observed it.
Q. Do you consider yourself to be an expert in talc mining and milling?

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MS. O'DELL: Objection, asked and answered.
A. No, I don't.
BY MR. ZELLERS:
Q. You have no independent basis to say that cosmetic talc contains asbestos, correct?
MS. O'DELL: Object to the form.
A. What do you mean by independent basis?
BY MR. ZELLERS:
Q. You have not done any testing of talcum powder to determine whether it contains asbestos or not; is that right?
A. No. All of my understanding is based on other sources.
Q. And those other sources would be, in part, the testing that was done by Longo; is that right?
A. Yes, as well as the testing that's reported in the -- in the literature section as the Imerys test results and quality control materials.

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Q. You're looking now back at the Pier Exhibit Pier-47 and the Hopkins Exhibit Hopkins-28; is that right?
A. I was actually referring to the Imerys documents that are referenced toward the end of the literature exhibit to my report, but certainly the Exhibit Pier-47 would be included there.
Q. You have no independent basis to say that cosmetic talcum powder contains fibrous talc, correct?
MS. O'DELL: Object to the form.
A. I have no independent basis, no.
BY MR. ZELLERS:
Q. You're familiar with the limitations of the research on a potential link between asbestos and ovarian cancer; is that right?
MS. O'DELL: Object to the form.
A. I'm familiar with some research limitations in that question, yes.

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BY MR. ZELLERS:
Q. You agree that research on the potential relationship between asbestos and ovarian cancer has only considered a small number of cases; is that right?
MS. O'DELL: Object to the form.
A. Well, it's considered thousands of cases. Certainly in terms of the number of women who have experienced ovarian cancer it's small, but it's significant, and that's where we get research from that answers important questions.
BY MR. ZELLERS:
Q. Are you familiar with the Reid paper, 2011?
A. Yes, but it's been a while since I've looked at it.
Q. Well, I'll hand you a copy. We'll mark it as Exhibit 17.
(Carson Deposition Exhibit 17 marked.)
MS. O'DELL: Thank you.
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BY MR. ZELLERS:
Q. The Reid paper that I've handed you, what we've marked as Exhibit 17, looks at the issue: Does exposure to asbestos cause ovarian cancer.
Is that right?
A. Yes.
Q. They talk about in terms of limitations on the first page, right-hand column, they say: Studies that have examined this issue have been limited for two major reasons.
Is that right?
A. Yes.
Q. Number one, small number of cases, much fewer women than men have been exposed to asbestos, particularly in more heavily exposed occupational settings where relative risks are higher; is that right?
A. Yes.
Q. How many of these studies -- well, strike that.
Would you agree that the studies in this area have been primarily

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related to occupational exposure?
A. Primarily, yes.
Q. How many total women have been studied?
MS. O'DELL: Object to the form. In this study, in this paper, or are you talking about in general?
MR. ZELLERS: In general.
A. I don't know the answer to that.
BY MR. ZELLERS:
Q. How many women have been studied in nonoccupational studies?
A. Well, very few in comparison to the occupational studies.
Q. Are you aware of the difficulties that have existed over time in distinguishing between peritoneal mesothelioma and ovarian cancer?
A. Yes.
Q. What are those difficulties?
A. There is a potential misclassification of one as the other because they have very common habits. They look very

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similar under light microscopy, and they're often difficult to distinguish, even by a pathologist, unless special tests are used.

Often these cases occur in places where they don't have the access to special test equipment that can definitively distinguish, and so they are classified and we move on.

Q. Another limitation of any studies in this area relate to the inability to account for nonoccupational risk factors for ovarian cancer other than age; is that right?

MS. O'DELL: Object to the form.

A. Are you reading also from this paper or --

BY MR. ZELLERS:

Q. I was looking now at the Camargo paper. Are you familiar with the Camargo paper?

A. If you have a copy of that, I'd like to look at it, if I'm going to answer questions about it.

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Q. All right. This is a paper in 2011. We'll mark it as Exhibit 18.

(Carson Deposition Exhibit 18 marked.)

BY MR. ZELLERS:

Q. Here the authors also looked at the issue of occupational exposure to asbestos and ovarian cancer; is that right?

A. Yes.

Q. If you turn to page 216 -- I'm sorry, 1216, second-to-last paragraph before the conclusion: A further limitation of our analysis was its inability to account for nonoccupational risk factors for ovarian cancer other than age.

Is that identified by the authors as a limitation?

A. Yes, it is.

Q. Under -- if you go a page back, 1215, under Discussion, in the second paragraph, the authors talk about other studies that have been done in this area, including Edelman; is that right?

MS. O'DELL: If you need to

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take a minute to refresh yourself on the page --

MR. ZELLERS: I'm looking under Discussion.

MS. O'DELL: -- please feel free to do that.

Excuse me, sir, I was talking. If you need to review the paper, Dr. Carson, please feel free to do that.

MR. ZELLERS: This doctor has given 35 depositions. He is perfectly capable of handling himself. He does not need your advice as we go along.

MS. O'DELL: Nor do I, Michael. So I'm going to deal with this witness in the way I choose, which is perfectly appropriate. If Dr. Carson needs to review the paper, he's going to review the paper. You may ask him questions, he'll be happy to respond.

MR. ZELLERS: Your job is not to coach the witness; your job is to make objections as to form or

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foundation, not to make speaking objections and coaching of the witness.

MS. O'DELL: If you have a question, I'm sure Dr. Carson would be happy to address it.

MR. ZELLERS: I've asked him the question.

MS. O'DELL: Would you mind repeating the question, please?

MR. ZELLERS: Sure.

THE WITNESS: I don't remember the question.

MR. ZELLERS: Okay. I'll be happy to repeat it.

BY MR. ZELLERS:

Q. Dr. Carson, you've looked at this Camargo paper; is that right?

A. Yes.

Q. In their discussion, they talk about other research, including research done by Edelman; is that right?

A. Are you at the top of the middle column on --

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Q. I'm looking under Discussion.
A. Yes.
Q. The first -- well, the second paragraph.
A. Second paragraph, yes.
Q. The magnitude of the pooled estimate is similar to that reported by Edelman; is that right?
A. Correct. Correct.
Q. Then they state: They concluded, however, that despite the positive and significant association, there was insufficient information to infer that ovarian cancers were caused by occupational exposure to asbestos because of concerns about tumor misclassification, inappropriate comparison populations and the failure to take into account for known risk factors.
Did I read that --
A. You read that correctly.
Q. All right. Are women who use talc perineally at greater risk of mesothelioma?
A. I can't say that they are, but

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they may be.
Q. Wouldn't you expect to find higher rates of other cancers in women using talc like mesothelioma if they are being exposed to substantial amounts of asbestos?
A. Well, we may -- we may be seeing some mesotheliomas that are misclassified as ovarian cancers, or we may be seeing mesotheliomas and not relating talc application as a pertinent contributor to that case.
Q. You told us earlier that you thought that there may have been more asbestos in talcum powders in the 1970s; is that right?
MS. O'DELL: Objection to form.
A. I think I said there have been step-wise improvements, and I -- but I agree with that statement.
BY MR. ZELLERS:
Q. Shouldn't we have seen higher rates of ovarian cancer in the earlier studies --
MS. O'DELL: Object --

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BY MR. ZELLERS:
Q. -- if your theory is correct?
MS. O'DELL: Object to the form.
A. There may have been higher rates of ovarian cancers, but you have to also understand that the latency period for ovarian cancer is pretty long. It's greater than 20 years, often as long as 40 years. And so we're still dealing with cancers that may have started back in the '70s.
BY MR. ZELLERS:
Q. Would you agree that exposure to asbestos through a perineal cosmetic talc use is different from the heavy occupational exposure that has primarily been researched?
MS. O'DELL: Objection to form.
A. Yes. I agree with that.
BY MR. ZELLERS:
Q. Are you an expert and knowledgeable about cleavage fragments?
A. I'm not.
Q. If I went through a series of questions and asked you to differentiate

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between cleavage fragments and asbestos fibers, you would defer that to other experts?
A. I would.
Q. You also claim that the presence of carcinogenic metals, including chromium, cobalt and nickel in talc, adds to its carcinogenicity; is that right?
A. That is right.
Q. Do you have an opinion or knowledge as to the amounts of chromium, cobalt and nickel, if any, in talc?
A. Those metal elements are included as -- usually as impurities or in very small quantities in some deposits and are present in small amounts.
Q. Do you have any idea how much of these metals, if any, reaches a woman's ovaries each time they use talc?
A. I can't tell you how much, but I can tell you that some does, and it is -- it remains in the talc until long after it reaches the ovaries.
Q. Chromium, cobalt and nickel are

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natural elements; is that right?
A. Yes.
Q. They are naturally in our bodies; is that right?
A. That's correct.
Q. They are present in food, drinking water, bottled water, vitamins; is that right?
A. To some extent.
Q. Do you have any evidence that the blood or tissue levels of any trace heavy metals are higher in genital talc users compared to nonusers?
MS. O'DELL: Object to the form.
A. I do not.
BY MR. ZELLERS:
Q. As we discussed when we talked about asbestos, you cannot evaluate the potential effects of exposure to a substance without factoring in the amount of exposure; is that right?
MS. O'DELL: Object to the form.

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A. It's useful to factor in the amount if the amount is known. If the amount is not known, it's not necessarily required to draw conclusions.
BY MR. ZELLERS:
Q. In this case, you do not know the amount, be it chromium, cobalt and/or nickel; is that right?
MS. O'DELL: Objection to the form.
Excuse me. Dr. Carson, as you know, is not being offered as a case-specific expert, so that question sounds like a specific patient, and so I would -- that's my objection.
A. I do not know the amount, but my opinion is that any within the microenvironment of the inflammatory process that is occurring due to talc sequestration is contributing to the carcinogenic potential.
BY MR. ZELLERS:
Q. But you don't know for any individual plaintiff their level of exposure

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to chromium, cobalt or nickel or any other heavy metal; is that right?
A. That is correct.
Q. That answer to that question would be true if I asked you about the different fragrance chemicals, correct?
MS. O'DELL: Object to the form.
A. Also true.
BY MR. ZELLERS:
Q. You did a risk assessment in this matter; is that right?
A. Yes.
Q. Do you agree that a complete and proper risk assessment involves four elements?
MS. O'DELL: Object to the form.
A. Not necessarily.
BY MR. ZELLERS:
Q. Well, you have to identify a potential hazard; is that right?
A. Yes.
Q. You've got to do some type of

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dose-response assessment; is that right?
A. Not necessarily.
Q. You --
MS. O'DELL: Excuse me. If you finished -- if you need to, Dr. Carson, if you're not finished. If you're finished, fine. Sorry.
A. A qualitative risk assessment does not necessarily require a dose-response in order to reach valid conclusions.
BY MR. ZELLERS:
Q. It is not necessary to do a dose-response assessment as part of a risk assessment. Is that your testimony under oath?
A. It's not always necessary.
Q. Was it necessary in this case?
A. Well, I think there is an aspect of dose-response that was performed in the risk assessment process here.
Q. What dose-response assessment did you make with respect to chromium, cobalt and nickel and any other heavy metal?
A. There's no information

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available to do a dose-response estimate for those metals.
Q. What information did you rely or use, if any, to make a dose-response assessment with respect to any fragrance chemicals?
MS. O'DELL: Objection, form.
A. There is no information available to do a dose-response estimate for the fragrances.
BY MR. ZELLERS:
Q. Did you do any type of exposure assessment in this case?
MS. O'DELL: Object to the form, vague.
A. I'm not sure exactly what you're -- what you're asking by exposure assessment.
BY MR. ZELLERS:
Q. Well, an exposure assessment is also part of a risk assessment; is that right?
A. In this risk assessment, I considered studies that are reported in the

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scientific and medical literature which have reported the assessment of exposure in these cases in various forms, and I considered those exposure assessments as being valid as reported and considered them as a whole.
Q. Did you look at any exposure assessment specific to the alleged heavy metals contained in talcum powder?
MS. O'DELL: Object to the form.
A. No, I did not.
BY MR. ZELLERS:
Q. Did you look at any exposure assessment with respect to any fragrance chemicals contained within talcum powder?
MS. O'DELL: Object to the form.
A. With respect to the fragrance chemicals and the heavy metals, the only exposure assessment that I was able to do was verify that these things were present in materials.
The fragrances are always present in whatever form they were added in,

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and the metals were there as the baseline component of the talc formation that they came from.
BY MR. ZELLERS:
Q. You do not know the amounts of either the heavy metals or the fragrance chemicals in the talcum powder at issue in this case, correct?
A. That's -- that's correct, I don't.
Q. You do not know -- well, strike that. I'll withdraw that.
You brought with you an IARC monograph; is that right?
A. I have a couple of them.
Q. All right.
MS. O'DELL: Are we going to -- are you going to move to --
MR. ZELLERS: We can take a break if you'd like.
MS. O'DELL: Yeah, it's been about an hour and a half.
MR. ZELLERS: Sure.
THE VIDEOGRAPHER: We're off

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the record 12:32, end of Tape 2.
(Recess taken, 12:32 p.m. to 1:38 p.m.)
THE VIDEOGRAPHER: We're on the record, 1:38, beginning of Tape 3.
BY MR. ZELLERS:
Q. Dr. Carson, when we left, we were talking about the trace metals and fragrance chemicals in talcum powder, correct?
A. Yes.
Q. You do not know how much of these trace metals or fragrance chemicals reach the ovaries, correct?
A. I don't know specifically how much reaches it, but if I know it's a component of the talc, and if I know the talc reaches it, then I know some of the metals and the fragrances reach it.
Q. You don't know the component or the amount of either the trace metals or the fragrance chemicals in the baby powder, correct?
A. That's correct.

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Q. You do not know the exposure of any of the women who are plaintiffs in this litigation to the talcum powder, correct?
MS. O'DELL: Individual women?
MR. ZELLERS: Yes, individual women.
A. I don't, no.
BY MR. ZELLERS:
Q. You brought with you an IARC monograph, and I think you've got several monographs that are on your literature list; is that right?
A. That's correct.
Q. Generally, IARC classifies chemicals and agents from Group 1, carcinogenic to humans, down to Group 4, probably not carcinogenic to humans; is that right?
A. That's correct.
Q. Does the classification of a substance as a known probable or possible carcinogen by IARC, and IARC is International Agency for Research on Cancer, or by the National Toxicology Program or the U.S.

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Environmental Protection Agency, mean that the substance can cause all types of cancers in humans by any exposure route?
MS. O'DELL: Object to the form.
A. No.
BY MR. ZELLERS:
Q. There are different cancers that may be associated with different chemicals or agents; is that right?
A. And different routes of exposure.
Q. You can have an agent that is a carcinogen or a probable or possible carcinogen for one type of cancer, but not for another type of cancer, correct?
A. That's correct.
Q. You can have an agent or a chemical that's a carcinogen for one route of exposure for a chemical or agent but is not carcinogenic for a different route of exposure, correct?
MS. O'DELL: Objection to form.
A. Yes.

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BY MR. ZELLERS:
Q. What -- would you agree that, in general, metals can differ in their toxicity and potential carcinogenicity based on their form?
A. Yes.
Q. Do you know the forms of chromium, nickel and cobalt detected in cosmetic talc?
A. There's -- metal ions are usually incorporated in the mineral lattice, and so they are part of the magnesium silicate crystal.
Q. I'm not sure if that answers my question, and if it does, I don't understand, so let me ask again.
Do you know the forms, and by that I mean valence state, of chromium or nickel or cobalt that have been detected in cosmetic talc?
A. Oh, the valence state?
Q. Yes, sir.
A. I don't know specifically, but that's dependent on the surrounding structure

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that the metals are contained in, and metals can assume a different valence state depending on the redox environment.
Q. You are not, at least in this litigation today, expressing any opinion as to the valence state of chromium that may be found in cosmetic talc, correct?
MS. O'DELL: Object to the form.
A. No, I'm not.
BY MR. ZELLERS:
Q. Your second opinion is that the perineal use of talcum powder results in direct exposure to the ovaries either via inhalation or migration through the female reproductive tract; is that right?
A. Well, it's primarily through the female reproductive tract. The inhalation exposure would be a secondary route.
Q. Let me ask you a couple of questions about inhalation exposure.
You do not cite any studies in the body of your report evidencing that

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talcum powder can reach the ovaries through inhalation, correct?
MS. O'DELL: Object to the form.
A. That is correct, although there -- yes, that's correct.
BY MR. ZELLERS:
Q. You have never performed any study yourself pertaining to whether inhaled talc can migrate to the ovaries; is that right?
A. I have not, although it has been used as an explanation of how talc particles might have reached the ovaries in persons who did not have another form of exposure.
Q. If inhalation is the exposure path for talc, shouldn't the lungs bear more of a burden?
A. Yes.
Q. Why, then, isn't there an epidemic of mesothelioma in women who use talcum powder?
A. Because the primary route is

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perineal via the reproductive tract.
Q. You discuss that on page 7 of your report; is that right?
A. Yes.
Q. You cite a number of studies for the proposition that talc can be transported from the perineum to the upper reproductive tract and body cavity; is that right?
A. That's correct.
Q. None of the articles that you cite actually looked at whether talc can migrate from perineal application through the fallopian tubes to the ovaries, did they?
A. Let me just refresh my memory for a moment here. Egli was carbon black. Venter was radioactive technetium labeled albumin. Let me see. Blumenkrantz -- I have my notes here.
Yeah, I can't remember what the substance was in Blumenkrantz. Sjösten, starch -- yeah, Blumenkrantz was retrograde menstruation. Halme was talc.
Q. Which study was talc?

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A. The -- I'm sorry. The Heller study was talc, which I didn't cite here. Halme was a retrograde menstruation study via the fallopian tubes, and Sjösten was starch particles.
Q. The only study -- and this is not one that you cited, but you've now referred to that involved talc, was Heller; is that right?
A. Well, it looked at -- it didn't look at transport inasmuch as it looked at the presence of talc particles in the ovaries and found them with or without the history of talc powder use.
Q. Heller looked at 24 patients; is that right?
A. I don't know, but that sounds about right.
Q. Half of them had a history of using talc products, half did not?
MS. O'DELL: Object to form.
A. That's correct.
BY MR. ZELLERS:
Q. Heller found talc in the

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tissues of all 24 patients; is that right?
A. That is correct.
Q. I believe we covered this before, but just to confirm: There are no published articles that you're aware of that show granulomas, fibrosis or adhesions anywhere in the reproductive tract of a woman as a result of external genital talc application, correct?
MS. O'DELL: Object to the form.
A. I believe that's the case, although there have been granulomas found in some cases of cancer where they reported having used talc.
BY MR. ZELLERS:
Q. Of the cases or the studies you cited here, Egli, that involved just three women, correct?
A. That was just -- that was an experimental study of the transport of carbon particles.
Q. The women were in a lithotomy position; is that right?

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A. That's correct.
Q. And that means that they had their legs up in the air, correct?
A. Correct.
Q. Those conditions -- well, strike that.
They were injected with oxytocin; is that right?
A. It is.
Q. That was to aid in the transport of the particles, correct?
MS. O'DELL: Object to the form.
A. I believe that was the author's theory.
BY MR. ZELLERS:
Q. Those are different circumstances or conditions from a woman who would apply a talc to her genital area standing up, correct?
A. Well, they are, but I'm not sure that that position is really pertinent to the migration of particles through the reproductive tract.

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Q. Is it your pos- -- is it your testimony that if a woman is in a lithotomy position with their legs up into the air, that that is comparable with respect to the migration of talc to a woman who's standing up and using it in her perineal region?
A. It may be.
Q. Are you an expert on that?
A. I'm not.
Q. The authors in Egli, they stated it was possible that the study observed false positives due to sample contamination because they failed to use liquid or filter blanks as negative controls, correct?
A. I don't recall that, but that may be the case.
Q. You refer to a study by Venter. That involved a radioactive particulate matter, correct?
A. Yes.
Q. Did not involve talc particles, correct?
A. The point of the study was --

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of all these studies -- that they were using various particles that could be detected at the other end, and so this was an attempt to do an experimental study which would cause no harm that would give them an answer regarding transport through the reproductive tract.
Q. In this study, particles were introduced into the reproductive tract, not externally; is that right?
MS. O'DELL: Object to the form.
A. That is correct.
BY MR. ZELLERS:
Q. Women were given Pitocin to stimulate uterine contractions; is that right?
A. That's the same as oxytocin.
Q. And that's a yes, correct?
A. Yes.
Q. Again, as with the Egli study, the women were inverted in the Trendelenburg position with their head down, legs up when the particles were administered; is that right?

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A. I believe so.
Q. Is it possible that the radionuclides can leach from the particles?
A. I don't know the answer to that, but it was radioactive technetium that was bound to albumin.
Q. The Sjösten study that you cite, that did not use -- involve the perineal use of talc, but an exam with a force to the cervix; is that right?
A. Excuse me. An exam with what?
Q. So it involved an exam with force to the cervix?
MS. O'DELL: Object to the form.
A. Well, this was -- this was done as an experimental study on women who were scheduled to get hysterectomies and they did it on some women one day prior to the hysterectomy and another group of women four days prior to the hysterectomy, and they used gloves that were powdered with starch and gloves that were not powdered with starch.
And so they had what's called a

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Latin square design, and they were able at the point of the hysterectomy of taking samples of the fallopian tubes and washing them to determine whether or not particles were found in the tubes.
BY MR. ZELLERS:
Q. What they actually found was that, whether the women were examined with gloves with the starch particles or not, they found starch particles in both, both groups, correct?
A. It is true.
Q. Tubal ligation, you refer to tubal ligation and use that or purport to say that that supports your migration theory, correct?
A. It does.
Q. Your testimony is that for patients who have had a tubal ligation, that they are at a lesser risk of the talc -- let me withdraw that.
Explain to us very briefly why you believe that tubal ligation supports your migration theory.

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A. If the pathway of exposure of the ovaries that results in ovarian cancer is via the reproductive tract, then tubal ligation, which closes off the fallopian tubes, would interrupt that pathway and result in reduced exposure; therefore, you would expect a reduced incidence of cancer in those women.
Q. In fact, though, that is not what has been reported or at least that has not been consistently reported in the studies; is that right?
A. Well, it actually has been a positive factor in a number of the epidemiologic studies that have looked at the ovarian cancer incidence and have been able to include tubal ligation as a historical factor in their analysis.
Q. Did you look at the Terry 2013 meta-analysis?
A. Yes.
Q. You cite that in support of your positions in this case; is that right?
A. I did.

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Q. In fact, in Terry -- well, and let me mark it for you so you've got it in front of you.
THE WITNESS: Okay. I'm going to move this binder for the time being, if you don't mind.
MR. ZELLERS: Oh, yes, I'll hand you the articles that I refer to, but if you need it, just pull it out.
THE WITNESS: Thank you.
(Carson Deposition Exhibit 19 marked.)
BY MR. ZELLERS:
Q. Deposition Exhibit 19 is the 2013 Terry meta-analysis that you referred to in your report; is that right?
A. Yes.
Q. That's a pooled analysis of eight studies; is that right?
A. Yes.
Q. Okay. This pooled analysis of eight studies relating to genital powder use and the risk of ovarian cancer shows no variation in the risk in talc users based on

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whether they had a tubal ligation or hysterectomy; is that right?
A. I think that's the conclusion of the authors here, but it's not the conclusion of the individual authors of the studies who did the original investigations.
Q. Well, it is the conclusion of the authors based upon their meta-analysis of eight studies; is that right?
MS. O'DELL: Object to the form.
A. Let me just check that.
(Document review.)
A. Yes.
BY MR. ZELLERS:
Q. If you look at pages 819, carried over to 820, I'm reading: Our finding of slightly attenuated associations following exclusion of women with powder exposure after tubal ligation or hysterectomy are not supportive of this hypothesis, but risk estimates in this subgroup analysis may have randomly differed from those including all women because of the reduction in sample

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size.
Is that right?
A. Yes.
Q. Essentially, looking at these eight studies in this meta-analysis, Terry did not find that exposure to genital powder applications that occurred before tubal ligation or hysterectomy made any substantive difference in the results; is that right?
A. Yes, but the point is that the authors didn't find that it did not make a difference either. They -- they ended up with a study with reduced numbers that they couldn't make determinations about.
Q. If, though, the migration theory is correct, you would expect that there would be a reduction in the incidence of ovarian cancer for women who have had a tubal ligation or hysterectomy; is that right?
MS. O'DELL: Object to the form.
A. Yes, that is correct.
///

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BY MR. ZELLERS:
Q. And that was not found in the Terry meta-analysis that you cite; is that right?
MS. O'DELL: Object to the form.
A. That is correct, but it was found in the baseline studies that were, in part, included in this meta-analysis.
BY MR. ZELLERS:
Q. Are you -- you also cite the Cramer study, 2016; is that right?
A. Yes.
Q. I've got a few questions for you on the Cramer study, but let me just ask, since we're at this part right now.
Do you have the Cramer study? I'll hand it to you.
A. If you have a copy, I'd appreciate it.
MR. ZELLERS: Sure. We'll mark the Cramer study as Exhibit 20.
(Carson Deposition Exhibit 20 marked.)

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THE WITNESS: Thank you.
MS. O'DELL: Thank you.
BY MR. ZELLERS:
Q. This is also a study, Exhibit 20, Cramer 2016, that you cite as supportive of your opinions in this case, correct?
A. Correct.
Q. Cramer actually looked at whether or not there was any greater association of talc use and ovarian cancer and whether or not women who had a tubal ligation or hysterectomy had a reduced incidence of the disease; is that correct?
A. Yes.
Q. Turn to page 337, and then it carries over to 339. They're talking -- they, being the authors -- of their results, and I'm reading just at the very bottom of 337, carried over to 339: By test for interaction, column 3, the association was significantly greater for women who were African-American, had no personal history of breast cancer, had a tubal ligation or

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hysterectomy.
Is that right?
MS. O'DELL: Object to the form.
A. Beginning on page 337?
BY MR. ZELLERS:
Q. Yes.
A. I'm sorry, if you could --
Q. Sure. At the very end of 337.
A. Okay.
Q. So they're looking at --
A. Oh, by tests for interaction.
Q. Yes.
A. Yeah.
Q. So if your migration theory is correct, you would expect there to be a lower incidence of ovarian cancer in women who have had a tubal ligation or hysterectomy, correct?
MS. O'DELL: Object to the form.
A. That is correct.
BY MR. ZELLERS:
Q. All right. Cramer finds by

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test for interaction the association was significantly greater for women who -- and then I'm skipping African-American, but I'm coming down to -- have a tubal ligation or hysterectomy.

Is that correct?

A. Yes.

Q. All right. If talcum powder migrates from the perineal region to the ovaries, shouldn't exposure to -- exposure to talc be far greater in concentration in the rectal, vulvar, vaginal, cervical and uterine tissues which are closer to the area of initial exposure?

MS. O'DELL: Objection to form.

A. Well, the acute exposure would be greater.

BY MR. ZELLERS:

Q. You would expect because the acute exposure is greater, that there should be inflammation caused in these organs and areas, correct?

A. No. The inflammation and oxidative stress is an ongoing process that

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has to develop over time, and it occurs on a chronic basis in areas where foreign bodies locate and reside. And talc and talcum powder are examples of foreign bodies that have the right characteristics to cause chemotaxis in reactive oxygen species and oxidative status.

Q. Well, in fact, there would be chronic exposure, so if we're dealing with, as you described in the very beginning, which you were asked, to look at the habitual use of talcum powder, that would create exposure on a chronic basis to the rectal area and tissues, vulvar, vaginal, cervical and uterine tissues; is that right?

MS. O'DELL: Object to the form.

A. I suspect if one doesn't bathe, that would be more of an issue, but most people bathe regularly as well.

BY MR. ZELLERS:

Q. And bathing regularly eliminates any exposure in the rectal, vulvar, vaginal, cervical and uterine tissues

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to talcum powder?

MS. O'DELL: Object to the form.

A. It doesn't -- it doesn't eliminate exposure, but it does remove residual exposure, as does sweating, other body secretions and so forth.

BY MR. ZELLERS:

Q. Are you aware of any studies that show inflammation or oxidative stress as a result of genital talc use in the rectal, vulvar, vaginal, cervical and uterine tissues?

A. No, I'm not.

Q. Under your theory or belief that talcum powder travels from the perineal region to the ovaries through the woman's reproductive tract, talcum powder must travel past the labia, through the vagina, through the cervix, and then to the uterus; is that right?

A. That's correct.

Q. And then the powder travels through the uterus and into the fallopian

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tubes to reach the ovaries; is that right?

A. Yes.

Q. On what studies are you relying to say that talcum powder affects the body differently when it's applied to the perineal region and travels to the cervix compared to when it is applied directly to the cervix?

A. I don't think --

MS. O'DELL: Object to the form.

A. -- there is much of a difference.

BY MR. ZELLERS:

Q. You would expect there to be a comparable similar result whether talcum powder is applied directly to the cervix through the use of dusting of a diaphragm as there is to the use of talcum powder in the genital areas; is that right?

A. That is correct. I think the two differ probably in terms of quantity very significantly. But other than that, they would be the same.

Q. When applied to the perineal

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region, talcum powder would also be in close contact with a woman's urethra; is that right?
A. Yes.
Q. Substances, and in your view, talcum powder, are capable of traveling up the urethra; is that right?
MS. O'DELL: Object to the form.
A. The urethra has a sphincter which prevents transport beyond that point.
BY MR. ZELLERS:
Q. Women get urinary tract infections when bacteria travels up the urethra; is that right?
A. That's correct.
Q. Studies, though, do not show an increase in bladder cancer with talcum powder use; is that right?
A. I don't believe that talcum powder transports in any appreciable amount up the urethra into the bladder.
Q. Studies do not show an increase in rectal cancer with talcum powder use, do

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they?
A. No.
Q. Are you aware that that IARC -- and you're familiar with IARC, right?
A. Yes.
Q. Are you aware that IARC rejects this migration theory and calls the evidence weak?
MS. O'DELL: Object to the form.
A. The IARC has made that statement in their -- I think the 2006 review that resulted in their recent monograph, but I think they're about to reconsider that.
BY MR. ZELLERS:
Q. Well, they also have stated that in 2010; is that right?
A. Well, that's the --
MS. O'DELL: Object to the form.
A. That's the monograph from the 2006 review.
BY MR. ZELLERS:
Q. Why do you believe that they're

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about to reconsider that?
A. Because the chatter is that this is something that's on their radar screen currently.
Q. What chatter are you aware of? And what is chatter?
A. It's discussion among -- within the scientific and healthcare community of things that are on the drawing board for IARC.
Q. Do you know whether or not IARC -- well, strike that.
IARC has not changed its position that the migration theory and evidence for the migration theory is weak; is that right?
MS. O'DELL: Object to the form.
A. They have not changed their position that was published in the 2010 monograph.
BY MR. ZELLERS:
Q. All right. You have heard chatter that they may look at it again; is

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that right?
A. Yes.
Q. Other than this chatter, you're unaware of any other -- well, strike that.
You're unaware of any change in IARC's position with respect to migration, correct?
A. Well, an example of what I'm talking about is the Health Canada report, which has contradicted what is found in the IARC monograph and is more current and considers information that will probably go into the next IARC review.
MR. ZELLERS: Move to strike as nonresponsive.
BY MR. ZELLERS:
Q. Does IARC review and rely on draft assessments in formulating their positions?
A. IARC relies on primary studies.
Q. Not draft assessments, correct?
A. Well, the draft assessment that I guess you're referring to, the Health Canada draft assessment, is derived from

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primary studies, the same ones that will be considered by IARC.
Q. All right. As of today, IARC's published position is that evidence of a migration theory of talcum powder migrating to the ovaries is weak, correct?
A. Yes.
Q. Have you conducted any tests or experiments with respect to your theory or position that talc migrates to the ovaries through the reproductive tract?
A. No, I haven't.
Q. How much talc actually reaches the ovaries in your opinion?
A. I can't answer that question because the dose has not been quantified.
Q. Does it only reach the ovaries during certain times?
A. I don't believe so. I think there are many circumstances whereby that migration pathway is functional, and in my belief, the pathway from the perineum to the cervix is pretty much an open channel, and then it continues to be open pretty much all

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the way into the pelvic cavity.
Q. You are not a specialist in women's health issues, correct?
MS. O'DELL: Object to the form.
A. Well, I'm a doctor. I've examined a lot of women.
BY MR. ZELLERS:
Q. Are you --
MS. O'DELL: Excuse me. Are you finished, sir?
THE WITNESS: Yes, I'm finished.
MS. O'DELL: Okay.
BY MR. ZELLERS:
Q. Are you an expert in the women's reproductive tract?
A. I've taken it apart and put it back together again in medical school, and in other settings I've done OB/GYN rotations. I've participated in pelvic surgeries. I understand the anatomy.
Q. There are physicians who are specialists in the female reproductive tract;

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is that right?
A. That is correct.
Q. You are not one of those physicians, correct?
A. I don't claim to be a specialist in gynecology.
Q. Your third opinion is that the ovaries lack an intrinsic elimination system; is that right?
A. That's correct.
Q. Is "intrinsic elimination system" a recognized term of art that's used by gynecologists?
A. I don't think so. It was just the term I used to describe the situation.
Q. Is "intrinsic elimination system" a term of art used by oncologists?
A. The same answer.
Q. Have you seen published studies that use that term?
A. I don't know. I suspect I could have. It's apparently a small number of ways to describe that in a few words.
Q. You do not cite to any studies

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in the body of your report to support your theory that the ovaries do not have an intrinsic elimination system, correct?
A. That's correct.
Q. You have not conducted any tests to show that exposure to the ovaries to particulate matter, if any, is longer than exposure to other parts of the female anatomy; is that right?
MS. O'DELL: Object to the form.
A. I have not conducted any such tests.
BY MR. ZELLERS:
Q. Is the cervix more or less sensitive to the impact of foreign particles than the ovaries?
MS. O'DELL: Object to the form.
A. I think that the important point is the residence time that exists, and the cervix is not presented with things for an extended time like the ovaries are in relation to things like talc. But it is

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sensitive.
BY MR. ZELLERS:
Q. All right. Your fourth theory -- or strike that.
Your fourth opinion is that the epidemiological studies show a positive relationship between regular perineal application of talcum powder and ovarian cancer; is that right?
A. That's correct.
Q. The studies that you reference in this opinion are referred to on pages 6 and 7 of your report; is that right?
MS. O'DELL: Object to the form.
A. Most of them, yes.
BY MR. ZELLERS:
Q. You conclude that when confounding and bias are exhaustively considered -- and do you believe you've done that here?
A. I am restating what authors of the primary studies have done. I'm evaluating the consistency of the evidence,

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not the basic evidence itself.
Q. The apparent cause and effect relationship between perineal talcum powder use and ovarian cancer amounts to about a 30% increased risk of ovarian cancer in talcum powder users.
Is that your opinion in this case?
A. It is.
Q. And that is your opinion from reviewing the epidemiologic studies that you cite in your report?
A. Yes.
Q. When epidemiologists refer to the statistical power of a study, what are they referring to?
A. Statistical power refers to the ability of a study design, if carried out, to detect a signal in the data of a particular magnitude.
Q. In plain English, statistical power is the likelihood that a study will detect an effect when there is an effect to be detected; is that fair?

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A. Yes.
MS. O'DELL: Object to the form.
BY MR. ZELLERS:
Q. Are you familiar with the term "person-years" as it relates to epidemiological study?
A. Yes, I am.
Q. What is -- strike that.
How are person-years calculated?
A. They are calculated by -- in relation to an exposure or to an existing treatment, they're calculated by multiplying the duration of the treatment or exposure in years by the number of people being studied. And that -- the result is person-years.
Q. Can you explain the difference between high-grade serous and low-grade serous cancer?
A. High-grade serous cancer has a -- is less differentiated and has a greater propensity for metastasis and invasion.
Q. Are you aware that the

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epidemiological literature shows that these are very different cancers?
A. They behave quite differently, yes.
Q. Do you know what publication bias is?
A. Yes.
Q. What is publication bias?
A. Publication bias is the tendency to -- to spin a certain argument in -- in order to influence acceptance of publications.
Q. Is that a recognized issue in the field of epidemiology, at least as you've observed?
A. It's a -- it's not necessarily recognized in the field of epidemiology. It exists in all scientific endeavors.
Q. Is it something that you and other physicians and experts and scientists need to be aware of?
A. Yes. I think we're all exposed to the effects of that and warned about it as we go through our careers.

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Q. When I asked you early on what your methodology was, you looked at the published literature, you looked at some websites I think that you told us about earlier, and then you performed a risk assessment and considered whether perineal use of talc products poses a safety risk to consumers; is that right?

MS. O'DELL: Object to the form.

A. Well, that's a gross oversimplification of the risk assessment process that I performed.

The review of the literature, which was based on the question that I was asked to address, was a fairly exhaustive one which incorporated a search for every pertinent publication that was available and included multiple languages.

It then was -- proceeded into a distillation of the facts that were -- that were claimed based on those individual studies and investigations, and a comparison of those, one with another, eventually

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considering them all as a whole to arrive at conclusions that addressed the question.

BY MR. ZELLERS:

Q. That was your methodology; is that right?

A. That is the methodology, yes.

Q. Did you consider the Bradford Hill criteria or factors in reaching your conclusions and opinions in this matter?

A. That's part of the methodology which is outlined in my report.

Q. In analyzing the Bradford Hill criteria, did you conduct a meta-analysis of the available data to reach a conclusion about the relative risk?

A. No, I did not.

Q. Why didn't you conduct a meta-analysis for this case?

A. I did not have the time to do a meta-analysis in this case, first of all. Secondly, there have been a number of other meta-analyses performed, and I had those results available to me in addition to various reviews of the literature that have

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been published as well. And I felt that was sufficient to be able to produce this report that addressed the question I was asked.

Q. As you told us earlier, you have never published a meta-analysis on any topic; is that right?

A. That's correct.

Q. You cite to some of the available studies on talcum powder use in ovarian cancer, but not to all of the studies, correct?

MS. O'DELL: Object to the form.

A. That's true.

BY MR. ZELLERS:

Q. What was your reasoning for focusing on certain studies and excluding other studies?

A. The studies that I referenced were those that had specific aspects that directly influenced my report or my conclusions or that I felt were illustrative of comments I was making in the report, and that's why they were referenced.

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All of the studies may not have risen to that -- the level of requiring being referenced, but pretty much all the studies are included in the literature that I reviewed.

Q. You cite in the report the studies that were favorable or supportive of your opinions, correct?

A. Well, I cited a number of studies, not all of which were favorable to my overall opinions, at least not on the surface.

Q. Did you cite all of the studies that you believe in one way or another support your opinions in this case?

A. I don't think so.

Q. You believe there are additional studies that support your opinions that you did not cite?

A. They're in the literature list.

Q. Did you cite the opinions that refuted -- strike that.

Did you cite the studies that refuted your opinions in this matter?

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A. I cited some studies that had opinions that -- or that had conclusions that did not necessarily agree with mine, but I don't think they refuted my conclusions.
Q. Do you believe the standard for proving causation in the scientific literature is the same one that applies in this litigation?
MS. O'DELL: Object to the form.
A. I don't know that.
BY MR. ZELLERS:
Q. A document you brought here today was an FDA letter?
A. Yeah, I think you marked it.
Q. I did mark it. Why don't you see if you could find it so I can ask you a couple of questions about it.
A. There it is. That one?
Q. Yes. Exhibit 10 is an FDA letter dated April 1st of 2014 to a Dr. Epstein; is that right?
A. Yes.
Q. That is a document that you

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reviewed and considered as part of your analysis of this case; is that right?
A. Yes.
Q. Do you believe that that exhibit, Exhibit 10, is supportive of your opinions in this matter?
A. I don't think it's very supportive. It's -- it's in response to a proposal from a citizens voluntary agency to provide more stringent labeling on talcum powder products, and the agency rejected the -- that petition.
Q. The FDA is the regulatory body in the United States that oversees food, drug and cosmetics; is that right?
MS. O'DELL: Object to the form.
A. Yes.
BY MR. ZELLERS:
Q. This letter -- strike that.
In this letter the FDA goes through and analyzes some of the Bradford Hill factors; is that right?
A. I'd have to look at this in

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more detail to be able to answer that specifically.
Q. Well, essentially, based upon its analysis as of 2014, the FDA concluded that causation had not been established as between genital talcum powder use and ovarian cancer or an increased risk of ovarian cancer, correct?
A. Well, it said that an updated review failed to identify any new compelling literature data or new scientific evidence. I don't think they indicate here that they actually did a standard review of that literature.
Q. Well, take a look, if you will, at page 4. The FDA sets forth its epidemiology and etiology findings; is that right?
A. Yes.
Q. The FDA has a number of very capable physicians, scientists, toxicologists, pharmacologists and medical professionals; is that right?
MS. O'DELL: Object to the

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form.
A. I don't know if they're still working, but they have good people on staff.
BY MR. ZELLERS:
Q. And just so, a year or two or three, if this transcript is ever reviewed, we are in the midst of a shutdown of at least portions of the government; is that right?
A. That's correct.
Q. And that is what your comment was directed to, correct?
A. That is correct.
Q. On page 4 the FDA states: After consideration of the scientific literature submitted in support of both citizens' petitions, FDA found.
And then, number 2, that several of the studies acknowledge biases in the study design and no single study has considered all the factors that potentially contribute to ovarian cancer, including selection bias and/or uncontrolled confounding that result in spurious positive associations between talc use and ovarian

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cancer risk.
Did I read that correctly?
A. You did read it correctly.
Q. Does that appear to be at least one of the conclusions of the FDA after considering the scientific literature as of early 2014?
MS. O'DELL: Object to the form.
A. Yes, that is listed as an FDI finding -- FDA finding.
BY MR. ZELLERS:
Q. The FDA noted that a dose-response -- strike that.
The FDA noted that dose-response evidence is lacking; is that right?
A. A dose-response --
Q. Two things. The FDA notes that there's a lack of consistency in the study results, correct?
MS. O'DELL: Where are you reading? I'm sorry.
MR. ZELLERS: I'm looking at

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Conclusion 3.
THE WITNESS: Point 3.
A. They found that the case-control studies did not demonstrate a consistent positive association across studies; although some studies have found small positive associations between talc and ovarian cancer, but lower confidence limits are often close to 1, and dose-response evidence is lacking.
BY MR. ZELLERS:
Q. That was FDA's conclusion number 3 based upon its review of the scientific literature; is that right?
MS. O'DELL: Object to the form.
A. It's correct. It's not a valid interpretation of the statistical results, but that was one of their findings.
BY MR. ZELLERS:
Q. Well, that was their finding. You disagree at least in part with their finding; is that right?
MS. O'DELL: Object to the

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form.
A. That is correct.
BY MR. ZELLERS:
Q. You are a paid expert for the plaintiffs in this litigation; is that right?
A. That is correct.
Q. To your knowledge, the FDA is not paid -- well, let me withdraw that.
A. I wouldn't go out on a limb there.
Q. Number 4, Conclusion 4, a cogent biological mechanism by which talc might lead to ovarian cancer is lacking. Exposure to talc does not account for all cases of ovarian cancer and there was no scientific consensus on the proportion of ovarian cancer cases that may be caused by talc exposure.
Was that a conclusion of the FDA based upon its review of the epidemiologic literature?
MS. O'DELL: Object to the form.
A. Yes, it was, and it's one that

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I also disagree with.
BY MR. ZELLERS:
Q. IARC also considered the Bradford Hill considerations; is that right?
A. Yes, it did.
Q. IARC rejected classification of talc as a carcinogenic, instead assigning it to the classification of possibly carcinogenic to humans; is that correct?
A. That's correct.
Q. We've already discussed the IARC categories briefly, but let's mark a document from the IARC website as to the classifications, Exhibit 21.
(Carson Deposition Exhibit 21 marked.)
BY MR. ZELLERS:
Q. Tell me if you recognize that.
A. Yes.
Q. Exhibit 21 is from the IARC website, and it goes through the classifications of different agents that have been made by the International Agency for Research on Cancer; is that right?

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A. Yes, that's correct.
Q. It has studied and included 120 agents in the Group 1 category, which is carcinogenic to humans, correct?
A. That's correct.
Q. That's the only category in which IARC finds sufficient evidence in humans, correct?
MS. O'DELL: Object to the form.
A. That's the category that represents substances for which there is sufficient and irrefutable evidence of human carcinogenesis.
BY MR. ZELLERS:
Q. It lists 82 agents in Group 2A as being probably carcinogenic to humans; is that right?
A. That's correct.
Q. IARC is certainly willing to declare agents as either a known or probable carcinogen; is that right?
A. That's correct.
Q. There is only one agent in

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Group 4, probably not carcinogenic to humans, correct?
A. Yes. I thought that number had gone up recently, but the date here is November 2018, so some may have been moved back into Group 3.
Q. So out of the over 1,000 agents that IARC has reviewed, it's only placed one agent in the Group 4 category, probably not carcinogenic; is that right?
A. That's correct.
Q. There is no Group 5, not carcinogenic; is that right?
A. That's correct.
Q. With genital talc, IARC Group 2B designation -- well, strike that.
Genital talc is listed as an IARC Group 2B designated substance; is that right?
A. That's correct.
Q. That's based on limited evidence in humans, which means that IARC cannot rule out chance, bias or confounding with reasonable confidence, correct?

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MS. O'DELL: Object to the form.
A. I think limited evidence also refers to just the number of studies that have been performed as well as the quality of the studies.
BY MR. ZELLERS:
Q. Well, based upon the evidence that is available, the studies that are available, a 2B designation by IARC means that IARC cannot rule out chance, bias or confounding with reasonable confidence, correct?
MS. O'DELL: Objection, asked and answered.
A. Not always the case.
BY MR. ZELLERS:
Q. That's part of the definition, isn't it?
A. I don't believe it applies to every agent or every evaluation.
Q. Well, I'll not take the time to go through the IARC definitions; if we at the end of the day have extra time, we'll go back

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and we'll take a look.
What else is in the Class 2B, possibly carcinogenic. Ginkgo biloba, is that something you're aware of that's in that category?
MS. O'DELL: Object to the form.
A. That's a biological material.
BY MR. ZELLERS:
Q. Pickled vegetables?
A. That may be in Group 2B.
Q. Occupational carpentry and joinery?
MS. O'DELL: Objection to form.
A. That's wood dust exposure.
BY MR. ZELLERS:
Q. Also 2B; is that right?
A. Wood dust itself is Group 1. The occupation is Group 2B.
Q. Let me ask you about some individual Bradford Hill criteria. On page 10 of your report, you state that you gave the most weight to strength of association, consistency and biologic

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plausibility; is that right?
A. That's correct.
Q. How much weight did you give to the other six factors?
A. Sufficient.
Q. Why did you put less weight on those?
A. Because the strength of association, the consistency of the evidence and the biological plausibility of perineal talc, talcum powder application as responsible for the occurrence of ovarian cancer was compelling.
Q. FDA focused on dose, correct?
A. Yes.
Q. You did not; is that right?
A. That's right.
Q. The first Bradford Hill factor that you focused on was strength of association.
What association does the literature report between talc use and ovarian cancer?
A. Overall, evaluating the

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universe of research, epidemiologic research that's been done on this, it shows an average 30% increase in ovarian cancer risk for those who regularly apply talcum powder to the perineum.
Q. Regular application of talcum powder means what?
A. It -- I believe that it means daily or thereabouts.
Q. In what form of application?
A. Talcum powder.
Q. In what amount?
A. Whatever is necessary or desired by the user.
Q. Does that vary from woman to woman?
A. It does.
Q. Did you make any attempt to assess what regular use of talcum powder was?
MS. O'DELL: Object to the form.
A. There have been a couple of attempts to try to quantify what -- what that means. I think for the most part they've

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been failed attempts, but they have been attempts to estimate the quantity of powder that you start with and the amount that results in the application to the perineum by using models and actually doing some measurements and recording activities.
BY MR. ZELLERS:
Q. You did not do any modeling or any assessment of the quantity of baby powder that was involved with daily use; is that right?
A. No, I relied on those others.
Q. When you say 30% increased risk, that's a 1.3 odds ratio; is that right?
A. That's correct.
Q. And that comes largely from the case-control studies, correct?
MS. O'DELL: Object to the form.
A. Yes, but it's also consistent with some of the information from the cohort studies.
BY MR. ZELLERS:
Q. Epidemiologists consider a 1.3

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odds ratio in a case-control study to be a weak or modest association; is that right?
MS. O'DELL: Object to the form.
A. That's correct.
BY MR. ZELLERS:
Q. Where here we're talking only about statistical associations, not causation, correct?
MS. O'DELL: Object to the form.
A. Well, association eventually becomes causation when the -- when the evidence mounts to a point where it becomes recognized by all of the players that this is what's going on.
A 30% increase may be classified by epidemiologists as weak or modest, but if you look at the number of women in this country who die each year from this fatal disease, that represents about 3,000 lives that could potentially be saved through prevention.
Q. There is not a --

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MS. BOCKUS: Excuse me, I need to object as nonresponsive.
MR. ZELLERS: Yes, join.
BY MR. ZELLERS:
Q. There is not a consensus at this time with respect to any causation relating to genital talc and ovarian cancer, is there?
MS. O'DELL: Objection to the form.
A. I believe that that consensus is building.
BY MR. ZELLERS:
Q. FDA -- that's not FDA's position, correct?
MS. O'DELL: Object to the form.
A. Not at the moment.
BY MR. ZELLERS:
Q. That's not the position of the National Cancer Institute; is that right?
A. That's correct.
Q. That's not the position of the CDC; is that correct?

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A. That's correct.
Q. IARC does not refer to any association between perineal talc use and ovarian cancer as a strong association, does it?
MS. O'DELL: Object to the form.
A. It calls it a Group 2B carcinogen, which is fairly significant.
BY MR. ZELLERS:
Q. Well, we discussed a few minutes ago that if an agent is a Group 2B carcinogen, that is based on limited evidence in humans; is that right?
A. That's correct.
Q. All right. Your opinions on strength of association, do they apply equally to all forms of ovarian cancer?
A. No, they don't. These apply to the epithelial ovarian cancer spectrum.
Q. Your opinions in terms of there being a -- well, let me withdraw that.
We've agreed that 1.3 is not a strong association, at least insofar as

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epidemiologists are concerned, correct?
MS. O'DELL: Object to -- object to the form.
A. It's an increased risk that translates into human lives, so it depends on your point of view.
MS. BOCKUS: Object to form -- I mean, sorry, nonresponsive, move to strike.
MR. ZELLERS: Join.
MS. O'DELL: Oppose.
DR. THOMPSON: Agreed.
BY MR. ZELLERS:
Q. The 1.3 relative risk that you believe generally applies, that would relate to epithelial cancers; is that right?
A. Yes.
Q. That's what you're limiting your opinions to in this case, correct?
MS. O'DELL: Object to the form.
A. Well, these opinions relate to several of the cancers that have shown increases in these background epidemiologic

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studies, which include the epithelial ovarian cancers, including the serous; the borderline cancers are also showing increases in some of the studies. So it's the group of those cancers, yes.
BY MR. ZELLERS:
Q. The cohort studies, prospective cohort studies, have not shown an association between talc and ovarian cancer, correct?
MS. O'DELL: Object to the form.
A. They have in some subtypes.
BY MR. ZELLERS:
Q. There was an initial description with respect to the first Nurses' study that was not supported in the update of that study; is that correct?
A. The Nurses' Health Study?
Q. Yes.
A. Yes, that's correct.
Q. Let's look at a different criteria, consistency. The literature does not show a consistent association between talc use and ovarian cancer, correct?

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MS. O'DELL: Object to the form.
A. I believe that, in fact, research shows -- does show a consistent pattern.
BY MR. ZELLERS:
Q. The cohort studies do not show an association between talc use and ovarian cancer as we just discussed, correct?
A. The basic cohort studies that look at all of the subjects and all of the cancers together typically do not rise to the level of significance.
Q. The hospital-based case-control studies collectively do not show an association between talc use and ovarian cancer, correct?
A. I sort of discount the distinction between the hospital-based studies and the community-based studies. I'm not sure whether there are valid reasons to consider those differently.
Q. We've discussed earlier that you are not an epidemiologist; is that right?

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MS. O'DELL: Object to the form, misstates his testimony.
A. I don't think I necessarily agreed to that characterization because I deal a lot with epidemiologic work. I'm a faculty member in the Department of Epidemiology at the University of Texas School of Public Health, and some may consider me an epidemiologist.
BY MR. ZELLERS:
Q. Do you consider yourself an expert in epidemiology?
A. No.
Q. Do you agree -- well, do you agree that hospital-based case-control studies are less susceptible to selection bias than population-based case-control studies?
A. It depends on the methodology that's used to recruit the study subjects.
Q. With hospital-based case-controlled studies, you're more likely to be comparing hospitalized patients to hospitalized patients rather than comparing

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ill patients in the community to healthy people in the community, correct?
A. In some cases that might be correct, but I'm not sure that's any -- in any sort of world an advantage.
Q. Well, shouldn't there be consistency if the Bradford Hill criteria is to be -- well, strike that.
In applying the Bradford Hill criteria of consistency, there should be consistency across different types of studies, cohort studies, hospital-based case-control studies, and population-based case-control studies, correct?
MS. O'DELL: Object to the form.
A. That's correct.
BY MR. ZELLERS:
Q. Isn't the absence of an association in the cohort studies especially significant in that the study design for the cohort studies reduces the likelihood of recall bias?
A. There are many forms of bias

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that study designers need to consider in the process of designing a study, and there are even more types of bias that are discovered after a study has begun.
You can fault case-control studies for being particularly sensitive to recall bias, but many of these authors who perform these studies indicated that they were well aware of that bias potential and took measures to avoid it.
The same thing can be said about cohort studies. They suffer from other forms of bias, misclassification in particular. They may also suffer from the fact that they are extremely expensive, have long duration, and require very large numbers of subjects in order to carry them out and are frequently underpowered and unable to arrive at the conclusions that they seek for that reason.
MR. ZELLERS: Move to strike as nonresponsive.
BY MR. ZELLERS:
Q. Is it possible that recall bias

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explains the difference between the cohort studies and the retrospective case-control studies?
MS. O'DELL: Object to form, asked and answered.
A. I don't believe that that is the case.
BY MR. ZELLERS:
Q. Is it possible?
MS. O'DELL: Objection.
A. Theoretically it would be possible.
BY MR. ZELLERS:
Q. Are you familiar with the Berge -- Berge 2017 study?
A. Yes.
Q. Is that a study that you cite and reviewed and rely on?
A. It was a meta-analysis.
Q. Is that a meta-analysis that you cite, review and have relied upon?
A. Yes.
Q. Take a look, if you will, at Exhibit 22.

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(Carson Deposition Exhibit 22 marked.)
THE WITNESS: Thank you.
MS. O'DELL: Thank you.
BY MR. ZELLERS:
Q. You're familiar with this meta-analysis; is that right?
A. Yes.
Q. The authors conclude that information bias from retrospective self-report of talc use is a possible explanation for the association detected in case-control studies; is that right?
MS. O'DELL: I'm sorry, are you reading from a certain page?
MR. ZELLERS: I am.
MS. O'DELL: Can you direct it to us, please?
THE WITNESS: Could you tell us where that is?
MR. ZELLERS: Sure.
BY MR. ZELLERS:
Q. Take a look if you will on page 6, the right-hand column, third

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paragraph. Reading from the second full paragraph, the authors discuss the fact that the association between genital talc use and risk of ovarian cancer is present in case-control but not in cohort studies, can be attributed to bias in the former type of studies; is that right?
MS. O'DELL: Object to the form.
A. That's what it says.
BY MR. ZELLERS:
Q. Then continuing down: Information bias from retrospective self-report of talc use is a possible explanation for the association detected in case-control studies.
Is that right?
A. That's what it says.
Q. What was your methodology for discounting the effect of recall bias in the population-based case-control studies?
A. The fact that several authors discussed the possibility of recall bias and incorporated methodology for avoiding recall

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bias, for example, placing parallel questions that should be affected in the same way, and still showed a positive result for talc and ovarian cancer is one reason.
The other has to do with consistency of the results, and although you've stated that from these various documents, including this quotation, that the case-control studies showed positive associations but the cohort studies did not, I would -- I would refute that by saying that all of the -- the vast majority of all of the studies show a positive odds ratio or relative risk, even if they don't rise to the level of significance.
If these results were obtained simply by chance, you would expect an equal number of positive results and negative results, but we don't have that here. We have practically all positive results with three or four outliers.
And so --
Q. We looked at the Taher paper early on in this deposition where Taher

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concluded that 15 out of the 30 case-control studies reported a statistically significant association between genital talc use and ovarian cancer, correct?
A. That's correct, but you're not -- you're not talking about the other 15.
Q. The hospital-based case-control studies collectively do not show a statistically significant association between talc use and ovarian cancer, correct?
MS. O'DELL: Object to the form.
A. I don't know that that is the case.
BY MR. ZELLERS:
Q. You don't know that it's not the case; you'd have to go back and relook at the studies, fair?
A. I'd have to look through here, which I'm happy to do if you want me to, but I don't believe that that's the case.
Q. In fact, the author, you cite the Langseth paper, a 2008 paper, as supportive of your position; is that right?

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A. Yes.
Q. I'll mark that Deposition Exhibit 23.
A. I think it was 2004, was it not?
Q. Well, I'm going to hand it to you and we can look at it together.
(Carson Deposition Exhibit 23 marked.)
A. Okay.
BY MR. ZELLERS:
Q. You're familiar with the Langseth paper; is that right?
A. Yes.
(Comments off the stenographic record.)
BY MR. ZELLERS:
Q. Langseth and the authors concluded that the current body of experimental and epidemiological evidence is insufficient to establish a causal association between perineal use of talc and ovarian cancer risk; is that right?
And I'm looking at the second

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page.
MS. O'DELL: Object to the form.
BY MR. ZELLERS:
Q. Is that the conclusion of the authors?
A. What I'm reading here is on balance, the epidemiological evidence suggests that the use of cosmetic talc in the perineal area may be associated with ovarian cancer risk. The mechanism of carcinogenicity may be related to inflammation.
Q. Take a look at the paragraph on the right-hand side under Proposal to Research Community. I'm looking at the second page of the Langseth article.
Are you there?
A. Yes, I am.
Q. The authors state: The current body of experimental and epidemiological evidence is insufficient to establish a causal association between perineal use of talc and ovarian cancer risk.

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Is that right?
MS. O'DELL: Object to the form.
A. That's what it says.
BY MR. ZELLERS:
Q. Experimental research is needed to better characterize deposition, retention and clearance of talc to evaluate the ovarian carcinogenicity of talc.
Is that what the authors state?
A. Well, that's what it says, but it says much more. In fact, the editors of the journal, in the section on the next page that is titled What This Study Adds, say: Epidemiological evidence suggests that the use of cosmetic talc in the perineal area may be associated with ovarian cancer risk. The IARC has classified this use of talc as possibly carcinogenic to human beings, Group 2B. The mechanism of carcinogenicity may be related to inflammation. This paper focused on the high degree of consistency in the studies accomplished so far and what should be the focus in future studies.

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So I --
Q. And then the conclusion is what I read, that: The current body of experimental and epidemiological evidence is insufficient to establish a causal association between perineal use of talc and ovarian cancer risk.
Correct?
MS. O'DELL: Object to the form.
A. That is what it says, but this was accepted in 2007, which was now 12 years ago.
BY MR. ZELLERS:
Q. Let me ask you about the cohort studies. They involved a much greater number of women than the case-controlled studies; is that right?
MS. O'DELL: Object to the form.
A. Well, they did not involve more cases, but they involved more women because in order to do a cohort study, you have to start with a huge group of people and wait

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for them to develop cancers, and then count those cancers.
BY MR. ZELLERS:
Q. What was your methodology for weighing the power of the cohort studies versus the case-control studies?
A. The cohort studies, it wasn't apparent in every research report exactly how they had done their sample size calculations and power determinations, but in many cases the lack of arriving at conclusions was simply due to an inability to detect an effect in the cohort studies, not that they detected that there was not an effect. And that's unfortunately a disadvantage of an underpowered study.
Q. Is it your testimony that the cohort studies are underpowered?
A. I think by and large most cohort studies are underpowered and -- because power calculations are based on chance. Investigators are sort of spinning the roulette wheel and hoping that the number that they want comes up. In some cases that

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doesn't happen.
Q. Is it your testimony that the cohort studies relating to genital talc use and ovarian cancer are spinning the roulette wheel?
MS. O'DELL: Object to the form.
A. In terms of the power of the studies to detect a meaningful difference among the subjects, yes.
BY MR. ZELLERS:
Q. That's your testimony as an expert in this case; is that right?
A. It is my testimony that cohort studies, including these, are chronic -- or quite often underpowered simply because of the expense associated with performing these studies.
Q. What analysis did you do to conclude that the cohort studies in this area, the four cohort studies, are underpowered?
A. Like I just mentioned to you, I read the studies and looked at their

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conclusions, and their conclusions were not that the effect didn't exist, but they couldn't detect it.
MR. ZELLERS: Let's go off the record because we need to change our tape.
THE VIDEOGRAPHER: We're off the record at 3:06, end of Tape 3.
(Recess taken, 3:06 p.m. to 3:19 p.m.)
THE VIDEOGRAPHER: We're on the record at 3:19, beginning of Tape 4.
BY MR. ZELLERS:
Q. Dr. Carson, you are not a statistician, correct?
A. That's correct.
Q. You are not a biostatistician; is that right?
A. That's right.
Q. Do you agree that some of the case-control studies have shown statistically significant findings and others have not?
A. I do agree that.
Q. If a study does not show a

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statistically significant association, it could mean that no risk exists, as we've discussed; is that right?
A. That's correct.
Q. What methodology did you use to weigh the lack of statistical significance across studies?
MS. O'DELL: Object to the form.
A. Across all of the case-control studies?
BY MR. ZELLERS:
Q. Yes.
A. I simply treated them as isolated research designs that were done on different populations in different places with different considerations. They were not necessarily comparable, like apples to apples or oranges to oranges; they were very different studies in most cases, and so I felt it was important to allow their findings to stand on their own.
Q. I want to talk to you about dose-response. That's another of the

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Bradford Hill criteria; is that right?
A. That's correct.
Q. Which studies show a dose-response, talc exposure and ovarian cancer?
A. Let me see here. I'm looking at my notes. The Harlow study from 1992 showed a dose-response, and the Cramer 2016 study showed a dose trend with strong odds ratios for premenopausal women and hormone therapy-treated women with greater than 24 years of exposure.
The Schildkraut study, also a case-controlled study of 2016, showed a dose-response.
Q. There are a number of studies that did not show a dose-response; is that right?
A. It's correct. They did not necessarily show there was not a dose-response. They just, as I was mentioning before, were unable to detect a dose-response.
Q. Do you have your report in

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front of you?
A. I do.
I would also add that the Penninkilampi meta-analysis also found a dose-response.
Q. Do you mention Penninkilampi at all in your report?
A. It's cited.
Q. In the body of your report?
A. I think it's in there somewhere.
Q. You believe it is; is that right?
A. I do.
Q. Well, I'll ask you a couple of questions about it then.
Before I do, let's talk a little bit more about your report. So go to page 7. You state at the very top of that page that it has been difficult to estimate dose in order to evaluate the dose-response relationship for ovarian cancer; is that right?
A. That's correct.

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Q. You state that it also has been difficult to exactly estimate the quantity of talcum powder administration during personal hygiene activities; is that right?
A. That's correct.
Q. Let's look at a couple of the studies that you believe do, in fact, show a dose-response. The Penninkilampi, that's a meta-analysis, 2018; is that right?
A. That's correct.
Q. That study does not consider or include the Gertic 2010 cohort study; is that right?
A. I -- I'd have to look at the table, but yes, that one may be left out.
Q. Well, that's a significant study to leave out of an analysis, isn't it?
MS. O'DELL: Object to the form.
THE WITNESS: I'm getting there.
(Document review.)
THE WITNESS: Apologies, I have binder block here.

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MS. O'DELL: You need help?
THE WITNESS: Okay.
BY MR. ZELLERS:
Q. And I misspoke. I meant to refer to Gates, the updated Nurses' study. So Gates 2010.
A. Yes, it appears that Gates is not included in the -- in the spectrum of studies considering; the Gertic study does appear.
Q. Gates 2010 is an important cohort study in this area, would you agree?
MS. O'DELL: Object to the form.
A. It's important, but I think it may be considered one of the ones that suffered from power issues. It wasn't able to determine a relative risk in the population that it assessed.
BY MR. ZELLERS:
Q. There are a number of the case-control studies that did not determine a relative risk, at least of statistical significance, correct?

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A. Well, they determined odds ratios, which is the equivalent of relative risk for a case-control study.
Q. And in a number of those case-control studies, at least 15 out of the 30 relative risk was not -- or strike that -- statistical significance was not achieved in the study; is that right?
MS. O'DELL: Object to the form.
A. That's correct.
BY MR. ZELLERS:
Q. Let's look at the Cramer paper. We've talked about this earlier.
A. Which one, the 2016?
Q. Exhibit 20, yes, 2016.
A. Okay.
Q. This is another study that you cite as being supportive of your dose-response opinion; is that right?
A. Yes.
Q. Tell me when you have it.
A. I think you may have picked up my copy or the copy that I was looking at.

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Q. This is my highlighted copy, so I'm sure it wasn't yours.
A. I'm sorry.
Q. That's all right. We'll -- take your time.
A. Here we are.
Q. Got it, Exhibit 20?
A. I think so.
Q. Do you have the Cramer study in front of you?
A. I do.
Q. It's a retrospective case-control study published in 2016; is that right?
A. That's correct.
Q. If we look at the table of results on page 337, Table 1.
Do you see that?
A. Yes.
Q. This table shows the risk of ovarian cancer for women who use talc, talcum powder, daily; is that right?
MS. O'DELL: Object to the form.

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A. It does.
BY MR. ZELLERS:
Q. And it's four different periods of time; one year, one to five years, five to 20 years and more than 20 years; is that right?
A. That's correct.
Q. There was only statistical significance found for the time period of one to five years of use and more than 20 years of use; is that right?
A. For the first group, the -- for those who reported months year of use -- months per year of use.
Q. Well, for the first group, which was equivalent to one year of daily use, there was no statistical significance; is that right?
MS. O'DELL: Object to the form.
A. That -- well, the -- there was a positive odds ratio with a nonsignificant 95% confidence interval.
///

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BY MR. ZELLERS:
Q. Meaning that if you look at this study, that it is certainly possible that because there is not statistical significance, there could be a finding of no risk, correct, no increased risk?
A. That's a possibility.
Q. Then if we go to the next period, we do show a dose-response for talcum powder use in the year -- years one to five; is that right?
A. Well, one to five years of daily use, yes.
Q. But then when we look at five to 20 years of daily use, there is not a statistically significant association; is that right?
A. That's correct.
Q. But then when we go to greater than 20 years, we do find a statistical association; is that right?
A. That's correct.
Q. If, in fact, there was a true dose-response relationship, you would expect

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to see that dose-response relationship in each of these groups; is that right?
MS. O'DELL: Object to the form.
A. It's more like we see in the group directly below that, where you start out with an odds ratio which is not significant but positive, and then reach a significant odds ratio at one to five years of daily use and a higher amount of significance with five to 20 years of daily use, and still a significant odds ratio, which is about the same level, at greater than 20 years of daily use.
BY MR. ZELLERS:
Q. Is that a yes to my question, that if you do have a true dose-response relationship, you would expect to see that dose-response continue throughout each of the periods?
MS. O'DELL: Object to the form.
A. Well, it would be nice if you did that, but epidemiologic data is very

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dirty, and it doesn't always work out quite that cleanly.
BY MR. ZELLERS:
Q. All right. Do you -- well, let me withdraw that.
Confounding. You considered and talk about confounding as another one of the Bradford Hill criteria; is that right?
MS. O'DELL: Object to the form.
A. Confounding, by that you mean specificity?
BY MR. ZELLERS:
Q. Well, I thought your -- I thought you said in your methodology that you applied the Bradford Hill criteria.
A. That's correct.
Q. Is confound -- strike that.
Is confounding an issue in interpreting epidemiologic studies?
A. Yes.
Q. Do you agree that there is confounding in these studies?
A. I'm sure there's confounding in

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these studies.
Q. You're familiar with that term, right?
A. Yes.
Q. That's where the presence of another association confuses the relationship between the exposure and the disease being studied; is that right?
A. That's correct.
Q. For example, if you're studying the association between coffee and pancreatic cancer, you need to be mindful of whether cigarette smoking is more common in coffee drinkers than the rest of the population, fair?
A. Yes.
Q. Coffee -- or strike that.
Cigarette smoking could be a confounder in that situation?
A. Possible.
Q. Because if more coffee drinkers are smokers than non-coffee drinkers, an association between coffee drinking and pancreatic cancer might be due to the

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smoking, not the coffee drinking; fair?
A. That would be a good description of confounding.
Q. Confounding can distort results in epidemiological studies; is that right?
A. It can.
Q. Do you agree that residual confounding is possible in every observational study?
A. Yes, I think there's some form of confounding that's present in every observational study.
Q. It's possible that unmeasured confounders may be present in every observational study; is that right?
A. That's correct. Not just unmeasured confounders, but unrecognized confounders.
Q. It's impossible to say that all known and unknown confounding factors have been controlled for in any given study; is that right?
A. I also agree with that.
Q. Many new factors possibly

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involved in ovarian cancer risk are just being published in the literature, correct?
MS. O'DELL: Object to the form.
A. I believe that is true.
BY MR. ZELLERS:
Q. For example, history of chlamydia infection, have you read about that possibly being involved in ovarian cancer risk?
A. I haven't read that specifically. I was thinking more about the new information regarding genetic susceptibilities.
Q. Also, weight gain during adolescence, is that another relatively new possible ovarian cancer risk factor?
MS. O'DELL: Object to the form.
A. It is, but obesity has been recognized as a cofactor for many years.
BY MR. ZELLERS:
Q. History of chlamydia infection, weight gain during adolescence, those were

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not controlled for in any of the talc/ovarian cancer studies, were they?
A. Not that I'm aware of.
Q. Are you aware that studies that show a relationship between talc and ovarian cancer did not account for confounders?
A. I think it's possible that many of those studies did not account for all potential confounders, but they made attempts to.
Q. For example, Terry 2013, we talked about that earlier; is that right?
A. Yes.
Q. Terry 2013, that meta-analysis did not adjust for hormone replacement therapy usage, correct?
A. Yes.
Q. If hormone replacement therapy is a risk factor for ovarian cancer, then the Terry 2013 meta-analysis did not account for that potential confounding factor, correct?
MS. O'DELL: Object to the form.
A. Correct.

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BY MR. ZELLERS:
Q. You cannot say whether the odds ratio of the Terry 2013 study would have been lower if the authors had adjusted for hormone replacement therapy usage, correct?
A. I cannot say that. Yes.
Q. Recall bias. You're familiar with recall bias?
A. I am.
Q. That is also a concern in every retrospective study, correct?
A. Yes.
Q. Recall bias can distort a scientific evaluation of whether an exposure is actually related to a disease; is that right?
A. Yes, it can.
Q. For example, recall bias could distort results if women with ovarian cancer were more likely to remember their exposure to talc than women without ovarian cancer; is that right?
MS. O'DELL: Object to the form.

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A. That's correct.
BY MR. ZELLERS:
Q. The effects of recall bias can be very real; is that right?
MS. O'DELL: Object to the form.
A. I'm not sure what you mean by very real.
BY MR. ZELLERS:
Q. Well, let's look at one of the studies that you cite. You cited the Schildkraut study in your report and you referred to it a bit earlier as supporting dose-response; is that right?
A. Yes.
Q. That's a study by Schildkraut and others titled Association Between Body Powder Use and Ovarian Cancer, the African-American Cancer Epidemiologic -- or Epidemiology Study.
Is that right?
A. Yes.
Q. I've got it here for you.
A. Okay.

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(Carson Deposition Exhibit 24 marked.)
BY MR. ZELLERS:
Q. Deposition Exhibit 24 is the Schildkraut study, 2016, correct?
(Pause.)
BY MR. ZELLERS:
Q. Did you say correct?
A. I think I did. I'm sorry.
Q. That's all right. I may have missed it.
Exhibit 24 is the Schildkraut 2016 study; is that right?
A. Yes.
Q. This is one of the studies that you cite to and that you relied on in forming your opinions; is that right?
A. Yes.
Q. The study looked at, among other things, what impact, if any, lawsuit filings in 2014 had on whether women recalled using talc in the past, correct?
A. I believe so.
Q. The authors thought that the

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publicity from lawsuits might influence the participants' recall of prior body powder use; is that right?
A. This was a recent study, so that was more likely.
Q. If you look on page 2, right-hand side, last paragraph that starts "Covariates include."
Do you see that?
A. Yes.
Q. And I'm reading about two-thirds of the way down: Two class action lawsuits were filed in 2014 concerning possible carcinogenic effects of body powder which may have influenced recall of use; therefore, year of interview 2014 or later, yes/no, was concluded as a covariate in the logistic regression models.
Is that correct?
A. That's correct.
Q. So go to page 4, Table 2. This is the adjusted odds ratio for the associations between mode, frequency and duration of body powder use in ovarian

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cancer; is that right?
A. Yes.
Q. The second column shows the number of cases, and that would be women with ovarian cancer; is that right?
A. That's correct.
Q. The third column shows the controls; that's the women who do not have ovarian cancer, correct?
A. Yes.
Q. Looking at this data before 2014, before the lawsuits, the percentage of controls, meaning women without ovarian cancer, said they used talc on their genitals was 34%; is that right?
So those are women who were interviewed before 2014.
A. Yes. Any genital use controls, 34%.
Q. And the controls, again, are women without ovarian cancer.
A. That's correct.
Q. The percentage of cases, meaning women with ovarian cancer, that were

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interviewed before 2014 that said they used talc on their genitals was 36.5%; is that right?
A. That's correct.
Q. So roughly the same reporting of genital talc use between women with and without ovarian cancer occurred for those women interviewed before the lawsuits were filed; is that right?
A. That's correct.
Q. Then look at what happened after the lawsuits were filed in 2014. For women interviewed after 2014, the percent of women without ovarian cancer that said they used talc on their genitals was 34.4%; is that right?
A. That's correct.
Q. So based on this data, the lawsuits had essentially no effect on how many of the women without ovarian cancer, the controls, remembered or recalled using baby powder; is that right?
A. Well, the percentage is the same in both cases.

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Q. It went from 34% to 34.4%; is that right?
A. That's correct.
Q. For women with ovarian cancer, before the lawsuits were filed, 36.5% of them said they recalled using baby powder; is that right?
A. That's right.
Q. But after the lawsuits were filed, the percent of women with ovarian cancer who said they used baby powder went up to 51.5%; is that right?
A. That is also correct.
Q. Is that a significant increase from 36.5%?
A. I don't know, but it seems like it might be.
Q. So after the lawsuits were filed, the percent of women with ovarian cancer who said they used baby powder jumped significantly; is that right?
MS. O'DELL: Object to the form.
A. Well, that's -- that is true.

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BY MR. ZELLERS:
Q. In this study, lawsuit filings appears to have affected how many women with ovarian cancer remembered using talc on their genitals but basically had no effect on the memory of women without ovarian cancer; is that right?
MS. O'DELL: Object to the form.
A. You can't say that this is -- this demonstrates recall bias. It could.
BY MR. ZELLERS:
Q. These findings could be an example of the potential effect of recall bias; is that right?
MS. O'DELL: Object to the form.
A. That is correct.
BY MR. ZELLERS:
Q. So pre-2014 there was an odds ratio of 1.19 with the confidence interval ranging from .87 to -- strike that -- from .87 to 1.63, so there is not statistical significance pre-2014; is that right?

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A. Probably not.
Q. If the study had been terminated as of 2014, prior to the lawsuits being filed, then the results of the study would have been that genital talc use was not statistically significantly associated with an increased risk of ovarian cancer; is that right?
MS. O'DELL: Object to the form.
A. Yes.
BY MR. ZELLERS:
Q. Did you make an attempt to account for this potential recall bias in weighing the Schildkraut study?
A. The authors did that for me by including the period of the interview as a cofactor in the logistic regression models. It accounts for this difference that you see on the table.
Q. You do agree there was no statistically significant finding of an odds ratio prior to 2014, the data collected through that time; is that right?

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A. In the -- in the data collected on those -- let me see here. In the data collected on those 351 cases and corresponding controls, there was not a significant odds ratio.
Q. I want to go back and ask you a few questions about some of the things I had talked to you before about.
In terms of this chatter about IARC, who has told you this?
A. There are a number of environmental websites and -- that also operate on social media that discuss this kind of thing.
Q. So there's social media websites that have talked about at least the possibility of IARC revisiting the issue?
A. Yes, among many other things.
Q. I asked you earlier about cornstarch, and you believe that cornstarch is rapidly cleared from the body, including the ovaries; is that right?
MS. O'DELL: Object to the form.

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A. Yes.
BY MR. ZELLERS:
Q. What is the mechanism by which you believe that cornstarch is rapidly cleared from the body, including the ovaries?
A. It's primarily composed of carbohydrate with a small amount of structural material, probably cellulose, and those materials are broken down in body fluids fairly rapidly and dissolved and become part of the general milieu of the body.
Q. Does cornstarch create inflammation in the body?
A. Yes.
Q. You testified that the latency period for ovarian cancer is between 20 and 40 years; is that right?
A. Roughly, yes.
Q. What is the basis for you saying that?
A. There are a number of factors that influence that, but there are organizations that have determined latency

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factors -- or latency periods for a number of different types of cancers and tumors based on the incidence data and what is known about the natural progression of those tumors over time.
I can't recall at the moment exactly where I determined the latency period for ovarian cancer to be between 20 and 40 years.
We do have a paper that's referenced here that discusses the determination of latency periods and includes ovarian cancer as one of the tumors that it determines a latency period for, and it uses a mathematical formula with various factors plugged into it to calculate that.
In that particular article, the latency factor -- period was very long. I think it was 44 years on the average.
Q. You do not have personal expertise in terms of the latency period for ovarian cancer, correct?
A. I have -- I've calculated latency periods as an exercise when I was in

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graduate school, but that's not something I normally do. I usually defer to the -- those who have published latency periods for that information.
Q. You are recalling that at least in some of the study or studies that you've reviewed that the latency period for ovarian cancer is 20 to 40 years, correct?
A. Yes.
Q. Are you able to tell us which study or studies you're relying on for that information?
A. I'd have to go through my list to find it. Do you mind if I take a moment to do that?
Q. Define "a moment."
A. Well, however long it takes me to find it in that list, but --
Q. Let me see if I can shortcut it.
Do you believe that the latency period for ovarian cancer is something you've written out in one of your handwritten notes?
A. I don't believe so.

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Q. It would be -- where would it be?
MS. O'DELL: If you need a moment to review either your report or your materials list, you know --
THE WITNESS: I don't believe that particular piece of information is in my report, but it's -- I think I could come up with it fairly quickly if I --
BY MR. ZELLERS:
Q. All right. Go ahead. Find for us the study or studies you're relying on for the latency period of ovarian cancer.
A. Okay. If I'm lucky, I may hit on it here.
(Document review.)
A. It's the Diana Nadler and Igor Zurbenko paper Estimating Cancer Latency Times Using the Weibull Model.
BY MR. ZELLERS:
Q. You're looking at Exhibit 4, your literature list; is that right?
A. Yes.

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Q. What page of Exhibit 4 are you looking at?
A. Page 17 in the Ns.
Q. Are you finished?
A. There may be others in the list, but you asked me to cite one. You want me to continue looking?
Q. No, I -- that is sufficient for my purposes. Thank you.
Dr. Carson, there have been some studies where talc particles had been observed or reported in the ovaries of women who have had perineal talc use; is that right?
A. Yes.
Q. Heller was one of the studies that we talked about, correct?
A. Correct.
Q. In those studies, there has not been inflammation noted; is that right?
A. No, there -- that's not been an important finding.
MR. ZELLERS: I have no further questions for you.

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MS. BOCKUS: If you want to pass me your microphone, I think I can stay here. I'm not going to pass him that many exhibits.
MR. ZELLERS: I'm happy to help you.
MS. BOCKUS: Thank you.
EXAMINATION
BY MS. BOCKUS:
Q. Dr. Carson, my name is Jane Bockus. I'm not certain I actually introduced myself to you this morning, but I represent Imerys in this litigation.
Do you understand that?
A. I do.
Q. Before Mr. Abney contacted you about preparing a report that would explain the relationship between regular perineal use of talc based on personal hygiene products and subsequent development of ovarian cancer, is that anything that you had researched before that date?
MS. O'DELL: Object to the form.

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A. I don't think Mr. Abney -- well, he may have been that detailed in our discussion. But in response to your question, that's not a specific question I had researched in the past, although I had researched related kinds of issues.
BY MS. BOCKUS:
Q. So would it be fair to say that the opinions contained in your report are all opinions that you have come to as a result of doing the research at the request of Mr. Abney and others in the plaintiffs' lawyer group?
MS. O'DELL: Object to the form.
A. Yes.
BY MS. BOCKUS:
Q. Okay. And I'm going to apologize right now. I'll be jumping around because most of my outline has already been covered, so let me just get you to look at your report, if I could, and I'm going to ask you some questions about it.
Turn to page 4, and

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paragraph (b), the first sentence reads: Numerous studies have examined the cancer-causing characteristics of talc.

Do you see that?

A. Yes.

Q. And you identified Wilde as your source for that statement, correct?

A. That is correct.

Q. Isn't it correct that the Wild study actually exonerated talc as having cancer-causing characteristics?

A. That was a conclusion of the author, but the reason it's cited there is because that's an example of the investigation of the relationship.

Q. Okay. But in that study, they -- he concluded that talc alone did not cause cancer, correct?

A. As I recall, that was the general conclusion, yes.

Q. Okay. Then in the next couple of sentences, you say that talc has caused cancer when implanted in various tissues and under the skin in laboratory animals. It

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causes inflammation and fibrotic reaction, including the chemotaxis of inflammatory immune cells and accelerated growth and division of cells in the involved tissue.

And you cite Okada 2007 for that proposition; is that correct?

A. That's correct.

Q. But Okada wasn't even looking at talc, was it?

A. Let me see here. Okada was looking at inflammation as -- as the endpoint in the various components of inflammation which I talked about here, the chemotaxis of inflammatory immune cells, accelerated growth division in the involved tissues.

Q. But what you say is that talc causes. When you say "it," you're referring to talc, correct? It causes inflammation and fibrotic reaction; isn't that what you're saying in this sentence?

A. It is talc, yes.

Q. Okay. And yet, Okada, the study that you cite for that proposition, doesn't look at talc at all, does it?

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A. No.

Q. And then going on, you talk about the fact that there in that same paragraph, if you go down, you talk about IARC and the fact that IARC concluded that talcum powder use by women for feminine hygiene is a possible human carcinogen; that's not a classification of talc as a carcinogen, correct?

MS. O'DELL: Object to the form.

A. It is within the spectrum of carcinogens.

BY MS. BOCKUS:

Q. It's possible.

A. That's correct.

Q. And then you say that -- meaning that there is insufficient evidence of carcinogenesis in humans, but strong evidence in other mammalian species.

Can you tell me where in IARC it says that there is strong evidence that talc causes ovarian cancer in other mammalian species?

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A. I think the issue is not specifically ovarian cancer; the issue is cancer. And that's the point of view of IARC, and that's what's alluded to here.

Q. So this is the one exhibit I'm going to hand you, if I can get that one marked by my assistant.

MR. ZELLERS: Exhibit 25.

(Carson Deposition Exhibit 25 marked.)

MS. O'DELL: This is a page out of the monograph?

MS. BOCKUS: Yes.

MS. O'DELL: Are you going to identify it?

MS. BOCKUS: And he can look it up in his whole monograph. I just pulled the page for simplicity.

MS. O'DELL: So feel free to do that, Doctor.

MS. BOCKUS: Yes, page 412.

BY MS. BOCKUS:

Q. So looking at Exhibit 25, this is a page from the IARC monograph where it

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talks about the data -- the evidence that they have and the evidence that they reviewed.
Do you see that?
A. That's correct.
Q. And what they actually state with regard to experimental evidence is that there is limited evidence in experimental animals for the carcinogenicity of talc not containing asbestos or asbestiform fibers.
Correct?
MS. O'DELL: Object to the form.
BY MS. BOCKUS:
Q. Did I read it incorrectly?
A. No, I just lost you for a moment.
Q. It's one sentence. Go ahead and take your time and read it.
A. Yes, I agree with that. They found that inhaled talc, which does not contain asbestos or asbestiform fibers, is Group 3.
Q. That wasn't my question. I'm

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talking about experimental animals because that's what -- you state in your report that IARC found strong evidence in animals, and yet the part of IARC that I know of where they're addressing the animal data with regard to talc is what I handed you in Section 6.2, and it states there's limited evidence, correct?
MS. O'DELL: Objection.
A. It states that there's limited evidence -- I need to find this section in the monograph. Just bear with me for a moment. It's page 412?
(Document review.)
A. Okay. I seem to be missing that part of the monograph.
MS. O'DELL: Do you have the 93 monograph?
THE WITNESS: Where's the -- this is 100C, and this is 93. Okay. Here it is. All right. Okay.
A. Okay. The entire monograph is designed to evaluate carcinogenic risk, and it looks at three different species, carbon

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black, titanium dioxide and talc.
So regarding talc, the overall point of view here is whether or not it produces cancer, not just ovarian cancer, not just lung cancer, but any cancer.
And so I'm not sure that that responds to your question.
BY MS. BOCKUS:
Q. No. My question was: You state in your report that IARC found strong evidence in animals, and I want to know where you believe that statement occurs in the IARC monograph, or do you know?
MS. O'DELL: And if you need a minute to look, feel free to do that.
A. Well, I can say that it might take me a while to look for it, but I can say that that's the basic definition of Group 2B, is limited evidence in humans and compelling evidence in animals or other --
BY MS. BOCKUS:
Q. Tell me where you're looking at that definition of 2B.
A. Let me see here.

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Q. We earlier marked the... Exhibit 21, I think.
A. Well, I have this other exhibit, which is the preamble from another situation; it's Exhibit P-346, and...
Q. Well, let me just ask a different question, rather than looking at the preamble.
A. All right.
Q. Because that's kind of overarching.
A. It is.
Q. To know what IARC found with regard to talc and the evidence in animal models, wouldn't it be more appropriate to look at what they actually said about talc in the animal studies?
A. Yes.
MS. O'DELL: Objection, form.
A. I would agree that that's the case.
BY MS. BOCKUS:
Q. And to your knowledge, nowhere did they find strong evidence of

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cancer-causing potential of talc in animal studies, correct?
MS. O'DELL: Objection to form.
A. Well -- well, it says on that page there's limited evidence in experimental animals, so I'll agree that at least in this location it does not say strong evidence.
BY MS. BOCKUS:
Q. And without going through the entire monograph, you don't know where that language came from, is that fair, that you used in your report?
MS. O'DELL: Object. Excuse me. Object to the form. I think he was pointing -- directing you to the preamble and you withdrew your question, but --
MS. BOCKUS: Well, let me just ask a qualifying question.
BY MS. BOCKUS:
Q. Does the preamble in any way address their findings with regards to talc?
A. No, the preamble addresses the methodology that's used by the IARC agency in

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addressing all the substances that they evaluate.
Q. Okay.
A. And that's usually where I pull things like that.
MS. O'DELL: Are you finished, Doctor?
THE WITNESS: Unless I'm going to continue to search for this.
BY MS. BOCKUS:
Q. I don't need for you to look in the preamble, because I'm really only interested in their findings as to talc, not their overarching methodology, that sort of thing.
A. Okay. But it's important to point out that this particular monograph is an evaluation of the carcinogenicity of talc that does not contain asbestos or asbestiform fibers, so --
Q. Correct. Which was, from their view, the talc that was included in all of the studies that they reviewed, correct?
MS. O'DELL: Objection,

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misstates the evidence.
A. I believe that was their assumption.
BY MS. BOCKUS:
Q. Okay. The studies that you reference in support of the notion that asbestos in -- that may or may not exist in body powder contributes to cause ovarian cancer, none of the studies that you cite to have referenced an application of a product to the perineum of the women and girls study, correct?
MS. O'DELL: Object to the form.
THE WITNESS: I have a -- I apologize greatly, but I lost the track. Could you repeat that question.
MS. BOCKUS: That's totally understandable because it was a little bit convoluted.
MS. O'DELL: Do you mind if we get the realtime running again? We're just off track here.

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MS. BOCKUS: That's okay.
BY MS. BOCKUS:
Q. I'm looking on page 5. Do you see on page 5 of your report, sir, paragraph (c)?
A. Yes.
Q. And there you cite one, two, three, four, five, six, seven, eight, nine, 10, 11, 12 studies, correct?
A. Yes.
Q. Do you speak Italian?
A. I can read it pretty well.
Q. Is that what you did for the Bertolotti study?
A. The Bertolotti study. Yes, I read most of it. I may have kibitzed with some of my colleagues about the meaning of a few words.
Q. At any rate, all of these studies have to do with heavy occupational exposure to asbestos, correct?
MS. O'DELL: Object to the form.
A. Yes.

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BY MS. BOCKUS:
Q. And you don't have any information how the dose of asbestos to which these women were exposed during their heavy occupational exposure compares to any exposure to asbestos from the use of body powder, correct?
A. Well, I think these were not all occupational exposures, but I do not have information regarding things like the route of exposure, no.
Q. Do you have any information regarding the dose?
A. No, I don't.
Q. Do you have any information that would compare the dose of asbestos to which the women in these studies were exposed --
A. Well, in some of the studies --
Q. Wait, I haven't finished my question.
A. Sorry.
Q. -- to any alleged dose of asbestos in body powder?

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Can you make any comparison whatsoever to the amount of asbestos to which these women were exposed to any exposure by any woman who has used a Johnson & Johnson body powder?
MS. O'DELL: Object to the form.
A. I don't think I'm able to make that kind of comparison.
BY MS. BOCKUS:
Q. Okay. There are ways to study whether two toxins combined increase a risk more than exposure to a single toxin, whether it -- whether one offsets the risk of one of the toxins or whether you add them together, even multiply them together, right?
A. Yes.
Q. Has any such study ever been done with regard to talc and the heavy metals that you identify in your report?
A. Not specifically a study to look at the combined contribution, but we know a lot about the mechanism of action of the metals in particular in the

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microenvironment, and based on what we know about the mechanism of action of talc as well and even asbestos, they're all similar, and for that reason would be expected to be additive.
Q. But the study hasn't been done even in a petri dish, has it?
MS. O'DELL: Object to the form.
A. I don't know if there's something in progress or not, but that's the kind of study that is currently being looked at. Combined exposures is the -- sort of the hallmark of research these days in toxicology.
BY MS. BOCKUS:
Q. Do you know of anyone who's looking at that question?
A. I don't.
Q. Okay. Have any of the heavy metals that you have identified been identified as carcinogenic to the ovary by IARC?
A. No.

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Q. I want you to turn to page 7 now, if you would, please, on other evidence. And you've talked about this paragraph a fair amount already, and I don't want to repeat any of the prior questions.
But I want to ask you about the statement in that first sentence, where you say that transport of talc-containing materials from the perineum to the upper reproductive tract and body cavities has been shown to occur with startling regularity. And I want to stop right there.
If I recall your testimony correctly, none of these studies even look at the transport of talc-containing materials from the perineum to the upper reproductive tract; isn't that correct?
MS. O'DELL: Object to the form.
A. Well, it is true that most of the research that's been done in this area has been done on materials that have been instilled into the vagina or the posterior fornix, but I think and it's my opinion that

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application to the perineum is equivalent to that.
Q. Do you have an opinion as to what percentage of the talcum powder applied in a daily dusting to the perineum makes its way to the vagina?
A. No, I don't know.
Q. Do you have an opinion as to what percentage of the talc that, in your opinion, would make its way to the vagina would actually make its way to the cervix?
A. I don't know that either.
Q. And out of the talc that makes its way to the cervix, what percentage makes it past the cervix into the uterus?
A. That, I don't know either.
Q. Do you have any reason to believe that talc would migrate with more frequency or rapidity than sperm?
MS. O'DELL: Objection to form.
A. No, I don't have reason to believe that would be the case.
BY MS. BOCKUS:
Q. Would you agree, in fact, that

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it is unlikely that talc, an inert particle, would travel as quickly or in the same percentages as sperm through the reproductive tract?
MS. O'DELL: Object to the form.
A. I think the transport time is roughly the same for any particulate matter, including sperm.
BY MS. BOCKUS:
Q. Do you have any studies to support that opinion?
A. Well, we know -- we know the -- we know the velocity of motile sperm; it's very slow. And we have studies that have shown the progression of particles through the fallopian tubes at at least that fast a rate, possibly faster.
And so the motility of sperm is slower than the rate at which it passes through the female reproductive system, so there are obviously other mechanisms at play other than sperm motility.
Q. To your knowledge, were any of

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those studies that you list here done in women who were standing up?
A. The studies that I list in other evidence?
Q. Yes.
A. I think not.
Q. In fact, were any of them done in women who were inclined with their head elevated over their hips?
A. No.
Q. So my question is: Where do you get the term "startling regularity" with regard to the transport of talc from outside a woman's body to the upper reproductive tract?
MS. O'DELL: Object to the form.
A. The propensity of evidence of rapid transport of particulate material regarding -- regardless of its composition.
BY MS. BOCKUS:
Q. Particulate material inserted well into a woman's vagina whose hips are above her head, correct?

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MS. O'DELL: Objection to form.
A. Well, we have other studies too. We have the powdered glove examination studies, things of that nature, that are a little bit different.
BY MS. BOCKUS:
Q. And you believe they support your conclusion that talc is transported from the perineum to the upper reproductive tract with startling regularity?
A. I think that's a valid conclusion supported by the evidence, yes.
Q. I'm turning to page 8 now, and the number that you have here -- and you've repeated it a couple of times today -- about your opinion that the elimination of talc as a risk could result in over 3,000 lives saved in the U.S. each year.
How did you come to that conclusion?
A. Well, I'm referring to talcum powder here --
Q. Okay. Sure.
A. -- which is the complete

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product.
I came to that conclusion based on the number of new cases of ovarian cancer that are diagnosed in the United States each year and the number of ovarian cancer deaths that occur each year.
And essentially, of 21,000 or so cases of -- new cases of ovarian cancer, there are corresponding 14,000 or more deaths each year, so that's a two-thirds fatality rate if you look over time.
The -- at 30% increase in the risk of -- or a 30% increase in the risk of cancer applied in reverse, that is reducing those -- that 30% increased risk from the use of perineal application of talcum powder could result in the prevention of as many as 3,000 lives, depending on the prevalence of use.
Q. Would that calculation require that 100% of the women in the U.S. be using talcum powder on a daily basis?
A. It would require a hundred percent of the women in the U.S. to stop

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using talcum powder on a daily basis.
Q. That wasn't my question.
In order to attribute --
A. Well, my answer to your question then is no.
Q. In order to attribute 30% of all ovarian cancer deaths to the use of talcum powder -- let me back up.
The data that you have that you've cited is talking about the percentage of women -- the percentage of women who use talcum powder who are diagnosed with ovarian cancer, correct?
MS. O'DELL: Object to the form.
A. It is the total number of new diagnoses per year.
BY MS. BOCKUS:
Q. Okay.
A. I think last year was 22,000-something.
Q. But that number, 22,000, 100% of those women did not use talcum powder, correct?

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A. There may not have been use of talcum powder in all those women, that's correct.
Q. Do you have any notion as to what percent of those women may have used talcum powder?
A. Based on these various studies, it seems to vary between 30 and 60%. It's more so in the U.S., Australia and the U.K.
Q. Do you have an opinion as to how regularly a women needs to use talcum powder before her risk of ovarian cancer is increased by 30%?
A. Well, based on the epidemiology studies, that risk occurs in the population in general from ever use as opposed to never use, and so it would depend on the individual woman.
Each person has an individual susceptibility and individual characteristics and would probably have an individual use pattern. So I couldn't say for any individual woman.
Q. And that's not what I'm asking

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for. I'm really asking for in general, because that's what epidemiology is, correct? It's not talking about an individual woman, right?
A. That's correct, it's describing it in the population.
Q. So in the population, in the studies that you've reviewed, what is the minimum number of days per month, or however you want to describe it, that a woman would need to use talcum powder before she would be included in the group that you believe have a 30% increased risk of ovarian cancer?
MS. O'DELL: Object to the form.
A. The only qualifier that I've been able to come up with and that I've used in this report is the regular use of talcum powder.
BY MS. BOCKUS:
Q. Okay.
A. And that is going to vary over a broad range. It would be periodically daily to several times a week would be

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regular use.
Q. And over how many years must a woman use talcum powder on a regular basis before her risk of ovarian cancer is increased to 30% --
MS. O'DELL: Object to the form.
BY MS. BOCKUS:
Q. -- in your opinion?
MS. BOCKUS: Sorry.
A. Some of the studies have focused on usage periods as short as one year, but most have studied longer periods of use and separated use into things like decades or accumulated total person-years based on reports of the women, multiplying frequency by time.
So again, it would depend on the individual, but the research reports hover around five to ten years of regular use, resulting in significant odds ratios.
BY MS. BOCKUS:
Q. As I understand it in toxicology, one of the basic tenets is that

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it's the dose that makes the poison, correct?
A. That's correct.
Q. That water can kill you if you drink too much of it, right?
A. Theoretically.
Q. In a short period of time.
And so I'm trying to find out what you have determined is the threshold of risk is -- for talcum powder use by women. Do you have an opinion as to at what point a threshold has been reached where the use of talcum powder by women in their perineal region increases their risk?
A. I think any use of carcinogenic materials or any exposure to carcinogenic materials increases the risk somewhat. A greater exposure, based on the "dose makes the poison" principle, would result in a greater risk.
And we know from toxicologic studies that intense exposures can sometimes accelerate the process and even shorten the latency period of a carcinogenic event.
So my opinion is that there is

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no threshold of exposure for risk; that we are -- we are right to use a zero threshold approach until we know more about the possibility of a threshold below which exposure would be safe. At the current time we don't have that information.
Q. Do you believe that there probably is a threshold below which use is safe?
A. In the carcinogenic process, which we haven't really talked about in this session today, there is an insult to a cell which affects the genetic material, the DNA. And there are built-in repair mechanisms that the cell has for fixing that problem that occurred, a mutation, for example.
These kinds of insults are happening to cells all the time, not just from carcinogens in our environment, but just from natural occurrences, even endogenous biochemical reactions cause these problems.
The question is: Is the repair process sufficient to undo what's been done? And an exposure to environmental carcinogens,

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that repair process is often overwhelmed so that it cannot catch up with the damage that's being created, and a tumor is born, basically.
That is where the concept of threshold comes from. Have we overwhelmed the repair or not, and we don't have enough research evidence or scientific evidence to be able to define that line at this point.
Q. Has there ever been a study that showed that talcum powder caused DNA damage in normal ovarian epithelial tissue?
A. Well, we do have the studies that have recently been produced by Fletcher and Saed that show the inflammatory process is influenced by talc, and this is nonfibrous talc, that result in mutagenic events that are available for promotion, and there are biomarkers that have also been established for that.
Q. The studies by Saed did not demonstrate DNA mutation, did they?
MS. O'DELL: Object to the form.

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A. I think they actually did.
BY MS. BOCKUS:
Q. That's your reading of them?
A. Yes.
Q. What Saed did is he placed talc on cultured ovarian cancer cells, correct?
A. Yes.
Q. And that actually -- what he recorded was an elevation in the CA-125?
A. That's one of the things he did. He also measured -- he did a number of genetic studies. He did transcribed RNA. He located individual SNPs, which are single nucleotide polymorphisms, in the genetic material.
And he found that as a result of that treatment, those mutations altered the effectiveness of antioxidant enzymes that are part of the protection mechanism and shield the repair process of the cell from further damage.
Q. Let's go back to the CA-125.
MS. O'DELL: If you need to pull the paper out, Doctor, just, if

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you want to take a moment and do that. I know you were searching for it while you were talking.
THE WITNESS: Yes, I think I have it right here.
MS. BOCKUS: These are just general questions that I'm going to ask you.
MS. O'DELL: You still may get the paper out.
MS. BOCKUS: Do whatever you want to do.
THE WITNESS: You can go ahead. I'm...
BY MS. BOCKUS:
Q. What controls did Saed use? Did he use any controls? In other words, did he place a known foreign object that was not -- that was known not to be a carcinogen on the cultured ovarian cells to see if there was a difference?
MS. O'DELL: Can you just pause just for a minute, let the doctor pull out the exhibit?

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THE WITNESS: I'm sorry, it appears that I do need to get the original paper here. There it is. Okay. Thank you.
(Document review.)
BY MS. BOCKUS:
Q. Can you answer the question: Did Saed have any either positive or negative controls that he used in his experiments?
MS. O'DELL: Object to the form.
A. I think he did, but I'd like to actually find it in here so I can give you the specifics.
Well, he used normal cells and epithelial ovarian cancer cells, and one was the control for the other. He treated them in the same way.
BY MS. BOCKUS:
Q. Let me ask a different question.
What I'm asking is: Did he use, say, glass beads to see if -- as a control to the talc? Did he have anything

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that he was controlling the cells' reaction to against the talc?
A. I don't believe so.
Q. That would be important in an experiment of this nature, would you not agree with that?
MS. O'DELL: Object to the form.
A. Well, he did utilize normal and cancerous cells, which would theoretically act as a control in that experiment.
BY MS. BOCKUS:
Q. That's not my question. I'm really asking about another element that he is exposing the cells to, both the normal and the cancerous cells.
MS. O'DELL: Objection to form.
BY MS. BOCKUS:
Q. To see if the reaction was just a reaction to a foreign body versus talc specifically.
Did he do that?
MS. O'DELL: Object to the form.

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A. I don't believe that he provided a control exposure as part of this experiment.
BY MS. BOCKUS:
Q. And you would agree that there are many things that will increase a CA-125, correct?
MS. O'DELL: Object to the form.
A. Yes, it's an acute-phase reactant.
BY MS. BOCKUS:
Q. Pregnancy can increase somebody's CA-125?
A. That's correct.
Q. And with regard to the SNPs, that is not the same thing as a test showing mutation, correct?
MS. O'DELL: Object to the form.
BY MS. BOCKUS:
Q. It's a surrogate.
A. Well, it's because there was transcribed RNA that was used to determine

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their presence, and the -- it's just part of their procedure, but it identifies genetic alterations. And those genetic alterations transformed into differential enzyme activities.
Q. Do you know whether there are standard tests for genotoxicity and mutagenicity?
A. There are lots of standard tests, yes.
Q. And Saed didn't use any of those, did he?
MS. O'DELL: Object to the form.
A. Well, he went directly to cells in culture to see what happened when they were treated with talc.
BY MS. BOCKUS:
Q. Does the amount of talc that Saed used compare in any way to the amount of talc that may reach a woman's ovary from perineal application?
MS. O'DELL: Object to the form.

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A. I don't specifically know.
BY MS. BOCKUS:
Q. There's no way to know that, is there?
A. No, there's not.
Q. Let me find my -- there we go. The Saed paper that you were looking at just a minute ago, it has something printed across it. What does that say?
A. In blue here?
Q. Uh-huh.
A. "For Peer Review."
Q. Okay. So it hasn't yet been peer reviewed; is that correct?
MS. O'DELL: Object to the form.
A. It's been submitted.
BY MS. BOCKUS:
Q. So does that mean it has not yet been peer reviewed?
MS. O'DELL: Object to the form.
A. I think it's been accepted for

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publication.
BY MS. BOCKUS:
Q. But the copy you have says on it "For Peer Review," correct?
A. That's correct.
Q. In the paragraph that we were looking at earlier, where you were talking about the startling regularity, later on in the paragraph you state that there is clearly -- sufficient particulate materials applied routinely to the perineum have ready access and in sufficient quantities to produce biologic responses in internal tissues.
What internal tissues have you seen any study recording a biologic response to talc from?
That was such a bad question, I'm going to ask it again.
What internal tissues are you referring to there?
A. Well, it says including -- including ovaries and surrounding structures. By surrounding structures, I'm referring to

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the fallopian fimbriae and the epithelium of the cavity.
Q. So -- and I know we've been through this already, but to your knowledge, there are no studies reporting biologic responses to talc in the vagina, correct?
A. Not that I'm aware.
Q. You're not aware of any studies reporting biologic responses to talc in the cervix, correct?
A. Correct.
Q. Are you aware of any studies reporting biologic response to the uterus?
A. No.
Q. Are you aware of any studies reporting a biologic response in the fallopian tubes?
MS. O'DELL: Object to the form.
A. Well, I don't -- I'm not aware of studies that draws a direct correlation between exposure to talc and reaction in the fallopian tubes.
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BY MS. BOCKUS:
Q. Okay. Is the ovary attached to the fallopian tube?
A. It is -- it's in the proximity. It's not directly attached.
Q. And what surrounds the ovary?
A. There's a structure that -- the ovary itself?
Q. Yes.
A. There's an epithelial membrane around the ovary, and --
Q. And then what touches the epithelial membrane?
A. Well, the fimbriae of the fallopian tubes surround that and the rest of it is just sort of space.
Q. Space. Is the space filled with fluid?
A. It is.
Q. And is that fluid kind of moving around?
A. All the time.
Q. All the time.
So things that come through the

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fallopian tube goes into that fluid and just gets moved around all the time; is that correct?
MS. O'DELL: Objection. Excuse me. Objection, form.
A. Well, there's a fairly direct presentation of the ovary, so there's not a large space there, but there is a space. And whatever goes into that space remains there. Some of it may come back out.
BY MS. BOCKUS:
Q. Does the fallopian tube move around during the month?
MS. O'DELL: Object to the form.
A. I don't know.
MS. BOCKUS: I'm almost finished. I'm going through all the things that I've crossed off.
BY MS. BOCKUS:
Q. So I understand you correctly, you have not identified a nonthreshold dose of talc; is that correct?
MS. O'DELL: Object to the

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form.
A. You mean a dose that is below a safe threshold?
BY MS. BOCKUS:
Q. Correct.
A. No, I have not.
Q. Did you make any attempt to extrapolate a de minimis risk level?
MS. O'DELL: Object to the form.
A. I did not. It would be nice to be able to do that, considering that most of us have had talcum powder exposures of one sort or another during our lives. And it's something that seems to have been felt to be very useful.
So it would be nice to be able to do that exercise, but I haven't -- I have not been prevented -- presented with the information to approach that, nor am I aware of anyone else who's been able to do it.
BY MS. BOCKUS:
Q. What information would you need that you don't have?

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A. Well, we'd need -- we'd need dose information, first of all, which we don't have, to combine with the epidemiologic results.

We need to define the mechanistic issues better than they are currently, and at that point I think we would be able to make some strong conclusions regarding potential thresholds of hazardous doses.

Q. You would agree that the great majority of women who use talcum powder on a regular basis are never diagnosed with ovarian cancer, correct?

A. I think that's true.

Q. And it's also true that the majority of women diagnosed with ovarian cancer have never used talcum powder on a regular basis, correct?

MS. O'DELL: Object to the form.

A. I think it's a majority, but there's a significant number who have.

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BY MS. BOCKUS:

Q. But the majority have not, correct?

A. I would say more than 50% have not.

Q. And would you agree that -- let me back up.

When is the last time you conducted a pelvic exam?

A. I haven't done one in a couple of years.

Q. Under what circumstances did you do it two years ago?

A. I see patients regularly, and in some cases, pelvic exams are either requested or indicated by the issue.

Q. It's not something you do on a regular basis, correct?

A. It's not.

Q. And you do not -- what percentage of your patients are women?

A. Probably half, maybe a little less than half.

Q. How do patients come to see

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you? In other words, are they referred by other people?

A. I have primarily a referral practice in toxicology.

Q. In toxicology? And so what types of patients are referred to you?

A. I have patients who are either workplace-related patients who have had chemical or other substance exposures. I also have a number of environmental exposure patients that I see.

And I also have a number of -- I also see a number of patients for general routine surveillance activities or required exams by regulation, either for licensure or certification.

Q. Are you sent patients where the patient is trying to figure out why they got some disease?

A. Sometimes. Usually the patient comes and tells me why they got the disease, and I go -- I talk to them about the possibilities, and we look at ways of confirming that or refuting it, or in many

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cases, altering to a correct path of diagnostic investigation.

Q. So sometimes a patient comes to you and says: I was exposed to this chemical and that's why I can't breathe?

A. Yes.

Q. And you do an investigation, and sometimes you say: You know what, that chemical has nothing to do with why you can't breathe?

A. Sometimes that's the case.

MS. O'DELL: Are you finished, sir? Are you finished?

A. Well, I just wanted to add --

BY MS. BOCKUS:

Q. Sure.

A. -- that although many times it is the case, and often the patient does understand that connection quite well, usually from a very closely connected cause and effect kind of relationship. It's when things are stretched out much more in time, and there is a likely suspect that may be an innocent bystander, that they may get

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confused.
Q. Have you ever been referred a patient to determine why they have ovarian cancer?
A. No.
Q. Do you know of any methodology accepted in the medical community for determining why an individual woman has developed ovarian cancer?
MS. O'DELL: Object to the form.
A. Other than genetic testing that identifies specific risks and history taking that might identify other known risk factors for that woman, there is -- I don't believe that there is any good or prescribed procedure for making that determination, and there is no reasonable screening test that can find that cancer when it is at an early stage.
BY MS. BOCKUS:
Q. Do you believe that obesity causes ovarian cancer?
A. It certainly seems to be

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related to the occurrence of ovarian cancer from a statistical point of view.
Q. What is the increase in a woman's risk of ovarian cancer if she's obese compared to a nonobese woman?
A. In terms of numbers?
Q. Yes, sir.
A. I don't know the -- I don't know the numbers.
Q. What other risk factors are you familiar with for ovarian cancer?
A. Well, certainly work with asbestos is a risk factor, and we have a number of studies that have shown women working in the asbestos industry or women who are married to asbestos workers and have secondary exposure presumably from that are at risk for ovarian cancer.
There are --
Q. Let me stop you just one second.
A. Yes.
Q. What percentage -- what is their relative risk or what is the odds ratio

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for that population of women?
A. Well, it varies depending on the research study that has been done, but I've seen odds ratios or relative risks all the way from 1 or even below to very high numbers, like 20 to 50.
Q. 20.0, is that what you're saying?
A. Yes, 20.0.
Q. Not 1.2, but 20.0?
A. Correct.
Q. Okay.
A. Which is a -- which would be 20 times the normal risk without the exposure.
Q. Okay. So we've got obesity and heavy exposure to asbestos. Any other risk factors that you're familiar with?
MS. O'DELL: Objection -- excuse me. Objection, misstates the doctor's testimony.
You may answer.
THE WITNESS: Okay.
A. Other risk factors for ovarian cancer would include things like early

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menarche, late menopause, never being pregnant. These are some of the more common risk factors that are identified.
There are genetic risk factors that are known, like the BRCA mutations, which confer an increased risk. Family history.
BY MS. BOCKUS:
Q. Do you know the odds ratios of any of the risk factors that you just identified of never having children, having early menarche or late menopause?
A. Right offhand, I don't know what those odds ratios -- the range of those are.
Q. Do you know if any of those odds ratios exceed 1.3?
A. I think they do.
Q. Does that lead you to conclude that those things cause ovarian cancer?
A. It certainly argues for that. The -- there's a risk factor that derives from something. You need a mechanism to fill in the blank.

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But also, some of these risk factors are so common in the population that we can concoct large cohort studies that will have -- can have very low relative risks, like on the order of 1.3 or even lower, and still a significant result.

So the more common a factor is, the easier it is to do the research and the more likely you'll get a finding that's relevant to interpretation.

Q. What pushes a talc particle from the perineum into the vagina?

A. Probably mostly the law of mass action. It simply goes of its own volition. These small particles are always in motion through molecular forces, and they simply move in all directions, and some of them move in that direction.

Q. Would that be true for any small particles applied to a woman's perineum?

A. Yes.

Q. Are you board certified in medical toxicology?

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A. I'm not. I started practicing medical toxicology before there was a board in the specialty, and I've been grandfathered into the profession as a member of the American College of Medical Toxicology.

Q. How long did you talk to Dr. Ness about her paper?

A. About her paper, probably a minute and a half. About all kinds of other things, for a while.

Q. What other kinds of things?

A. Mostly personal things that had nothing to do with talc or this case.

Q. How long do you think that conversation was?

A. Well, with Dr. Ness, nothing lasts very long, so I would say ten minutes at the most.

Q. Okay. Did you call her?

A. No. She's -- she comes and goes in the same building where I office, and my office is just on the opposite side of the floor of hers, and I see her sometimes in passing or in the elevator.

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Q. So you think you just ran into her?

A. Yeah.

Q. The other people that you identified that you discussed your report with, did you ask them to read your report?

A. I asked them to look at parts of it, early drafts of it to let me know if they thought I was making sense.

Q. And did they offer you comments and suggestions for changes in your paper?

A. Not really. Mostly they gave me a pat on the back and said: I think you're doing a good job, just sort of beef this part up, and what do you mean by this, maybe I could rephrase that. That sort of thing.

Q. Did they give you written suggestions?

A. No, these were all verbal comments.

Q. Had you given them a hard copy of the portions of your report that you wanted them to comment on?

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A. Yes.

Q. And they didn't redline it or make -- draw arrows or anything like that for you?

A. I think actually George Delclos did draw some -- or make some notes on there and hand it back to me, and I incorporated those into my electronic version.

Q. Do you still have George's notes to you?

A. No, I don't.

Q. Is he the only one out of the people that you asked to look at it who gave you handwritten notes?

A. Yes, I think so.

Q. Have you seen the term "intrinsic elimination system" regarding the ovary in any of the publications that you've read?

A. I don't know, I may have.

Q. Can you think of one in particular that discusses that characteristic of -- that you believe relates to the ovary?

A. Well, the migration papers

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discuss migration to the ovary. It would probably be a talc paper, though. I don't recall seeing it anywhere.
Q. Did you consult any gynecologic textbooks?
A. No, I didn't. I may have looked at some diagrams on the Internet.
Q. Okay. Did you consult any gynecologic oncology textbooks?
A. Not textbooks, no.
Q. Do you know the position of the Society of Gynecologic Oncologists on the question of whether does talc increase a woman's risk for ovarian cancer?
A. No, I don't.
Q. Would that be important to you to know their position?
A. No, I don't think so.
Q. Do you know the position of ACOG on whether the use of -- perineal use of talc increases a woman's risk of ovarian cancer?
A. I don't know that either. That's not something I've looked at.

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Q. Would that be important to you?
A. No.
Q. Do you have any scientific text that suggests that an inert particle resides on the ovary longer than it does in the cervix?
A. Well, I have -- I have a paper that relates to the time for dissolution of a particle in biological fluids, which would go to the length of time a particle of talc remains in the ovary once it gets there.
But I don't have -- I don't know that I have a scientific paper that specifically says that it stays in the ovary longer than it stays in the cervix.
Q. You testified that you understand there have been some attempts to quantify the amount of talc, I guess from a single use, that ends up on the perineum.
Did I understand that correctly?
A. Yes.
Q. Can you tell me what those attempts are, who did them, where did you see

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that?
A. Well, I saw this actually when I first started this process, and I think Dr. Longo was involved in that activity, where they modeled the -- the application of talcum powder and did some calculations based on the amount of substance that was used, and they measured it in things like shakes and -- and then quantified the amount that was lost from the container to determine what an application amount was.
I don't think they were able to go beyond that point in the modeling process.
Q. You didn't see anything that Dr. Longo did that attempted to quantify the amount of talcum powder from a single shake that ended up on a woman's perineum, did you?
MS. O'DELL: Object to the form.
A. I -- you know, I don't know the answer to that, simply because I don't recall, but I wouldn't be surprised that there was an attempt made to do that. But beyond that, I don't think anything would be

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successful.
These were clothed subjects, so that adds another factor to the calculation.
BY MS. BOCKUS:
Q. Is that the only experiment that you're familiar with that you've seen anywhere that attempts to quantify the amount of talcum powder from a single use that ends up actually on a woman's perineum?
A. There was another part of that study where they applied it to underwear with the same sort of calculation process. It was all part of the same modeling process.
Q. And do you recall what percentage of the talc applied to the underwear ended up adhered to the woman's perineum?
MS. O'DELL: Object to the form.
A. I don't think -- I don't think they measured the amount that adhered to the perineum. I think what they were interested in was proximity.
///

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BY MS. BOCKUS:
Q. Okay. Can you tell me the names of the environmental websites that have been talking about IARC revisiting their classification of talc?
A. There are -- there are a number of Twitter feeds and websites that carry on this kind of discussion. Science Interest is one of them. I think IARC Watch is another one. I have -- I get e-mails about some of these and end up going into them for a period of time and seeing if they have anything interesting going on. Some of them are searchable.
And then I get e-mails from the ones that I visit about other ones. So I spend as much of my time deleting these e-mails without reading them as I do actually viewing the material.
Q. So fair to say this is just chatter you've seen on the Internet in these different chat rooms or Twitter accounts that you visit from time to time?
A. It's all Internet based, yes.

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MS. BOCKUS: Okay. I think that's all I have. Thank you.
MS. O'DELL: Why don't we take a short break. We've been going about two hours.
MR. ZELLERS: Do you have questions?
MS. APPEL: I do, but --
MS. O'DELL: Yeah, do you have --
MS. APPEL: I don't have a lot.
MS. O'DELL: Okay. Sure. Why don't you go ahead, and then we'll take a break. We have been going about two hours, but, Renée, please.
If you're okay, Doctor.
THE WITNESS: I'm fine.
EXAMINATION
BY MS. APPEL:
Q. It's been a while since we did introductions, so just as a reminder, my name is Renée Appel and I'm here on behalf of Seyfarth Shaw and I represent Personal Care Products, counsel.

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A. Uh-huh.
Q. And echoing what my colleagues have said today, if there's at any point I ask a question that you do not understand, just stop me and ask me to rephrase it or let me know otherwise, okay?
A. I will.
Q. Thanks.
So going back shortly to your scope of work, do you teach any coursework on talc or ovarian cancer?
A. I teach some general courses. Up until last spring I taught a general environmental health course for graduate students in the Master of Public Health program at the School of Public Health, and in that course we did touch on things like environmental exposures that would include minerals of various varieties, but it was very cursory.
Q. And was that curriculum specific to environmental and industrial products or minerals as opposed to consumer products?

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A. We actually did touch on other consumer products as well in terms of the significant environmental problem that we have currently, but -- regarding the huge volume of personal care products that goes into our aqueous waste stream and how that's affecting the aquatic environment as well as groundwater and so forth.
As a matter of fact, in that course, as part of the culmination of the course, there are student workgroups that develop presentations on a particular topic, and the topic of personal care products has been a favorite choice for the last several years.
Q. But your curriculum did not include talc among those products?
MS. O'DELL: Object to the form.
A. I think talc may have been represented as an individual mineral on a slide that listed many minerals.
BY MS. APPEL:
Q. Earlier today you had mentioned

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a shared file. Is that shared file something that you created or plaintiffs' counsel created?

A. It's something that I think plaintiffs' counsel created for me to be able to send them documents and receive documents, and it's a Dropbox share file. It's -- at this point I think it might be mine. I'm not sure just exactly who's in charge of that or runs it, but it comes directly into my Dropbox file.

I know I had to boost my subscription to Dropbox in order to hold the 2 gigabytes of data from -- that we were putting into there.

Q. Is there anything from that Dropbox file that you relied upon in forming your opinion in your report that you have not already provided to defense counsel?

A. No, everything that was in that Dropbox that I've relied upon has been identified here.

Q. Who prepared Exhibit B to your report?

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A. Exhibit B was a list of articles from the research literature included in the Dropbox that -- that I think does not -- I don't know whether it includes the referenced articles from my report or not, but they were all part of the same collection of research articles and supplemental documents.

Q. And my question, Dr. Carson, was: Who prepared that exhibit?

A. The exhibit was prepared by the plaintiffs' attorneys.

Q. You testified earlier that you have spent approximately 150 to 180 hours in your expert retention work; is that correct?

A. Correct.

Q. Can you estimate what portion of that time was spent researching versus what portion of time was spent actually drafting your expert report?

A. Those two things are in some ways difficult to separate because I would -- I was writing my report the entire time that I was reviewing the research materials and

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accumulating information in the draft as a result of my review of the literature.

So if I had to separate things out, I would say that, by far, the -- most of the time has been spent in reading articles and reviewing them and comparing them with other articles, and a comparatively small amount of time has been spent in drafting the report.

Although there were some strings of activity which was all report drafting basically, I would say probably 85 to 90% was research, seeking articles, reading them, reviewing them, and comparing them.

Q. And you also testified earlier today that you discarded information not relevant or interesting to you.

How did you make that determination?

MS. O'DELL: Objection to the form.

A. The things that I discarded did not seem to fit into my gestalt of the

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understanding of this question and the opinions that I wanted to express. They may have been interesting information and useful for some purposes, but not for this particular report.

BY MS. APPEL:

Q. Was some of that information that you discarded based on relevancy or that you determined was not of interest information that may have been different than your opinions?

A. No. I didn't discard any research because the opinions provided differed from my own. These were things that really were irrelevant to the question.

I remember finding an awful lot of geological research stuff that just didn't have any relevance to the question.

Because I used such broad search terms, I ended up pulling in a whole lot of things that were not necessary or useful, and those just went in the trash.

Q. You testified earlier that you have not treated any patients with ovarian

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cancer; is that correct?
A. Not knowingly, not because of ovarian cancer.
Q. Have you ever diagnosed any patients with ovarian cancer?
A. I think when I was in medical school or residency, I probably participated in that on several patients.
Q. Have you ever instructed a patient not to use talcum powder products?
A. I hadn't up until a month or two ago, but I've been asking people about -- about their talcum powder use just as sort of a curiosity in mentioning that there might be a risk.
Q. Do you ask that of all your patients?
A. I would say no, I don't usually ask the men that, but I probably should.
Q. And have the responses to those inquiries of your female patients and their talcum product use, has that been used at all to inform your opinions in this case?
A. I don't think so. There have

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been very few that I have asked that question in the last month or so. I've had a limited clinic schedule during this period of time. We had the holidays and other things, so I haven't seen that many patients.
And of those I've asked about it, it seems about half of the women have had a history of using talcum powder.
Q. And of those women that are using -- have told you that they have used talcum powder, are those women diagnosed with ovarian cancer?
A. No.
Q. So suffice to say the inquiry that you've asked of your female patients concerning their talcum use has nothing to do with the question that you've been posed in this particular litigation?
MS. O'DELL: Object to the form.
A. Actually, that's the only reason I've been asking them. It's not something that came to mind earlier. I have an environmental exposure survey that I

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usually administer to my patients, and I have plans to add that as a question in my environmental exposure survey. Which I haven't done already, but will as soon as I get the opportunity.
BY MS. APPEL:
Q. You testified earlier today that you do not believe there was ever a point where talcum powder did not contain asbestos, correct?
A. Yes.
Q. So in forming your opinion in your report, you've assumed that the talcum powder does contain asbestos, correct?
MS. O'DELL: Object to the form.
A. Well, I think the asbestos contribution to this whole issue is important and significant. I think there's good evidence that whatever we call talcum powder is carcinogenic and responsible for ovarian cancer -- as a cause of ovarian cancer, but I can't say -- I can't say based on looking at a can of talcum powder whether or not it has

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asbestos in it or how much.
BY MS. APPEL:
Q. Have you formed an opinion, Dr. Carson, on whether there's a relationship between pure talc and ovarian cancer?
MS. O'DELL: Objection to form.
A. My opinion is there is, but that's based on the research reports that have been done using so-called pure talc, talcum powder, and I am -- I -- my opinion is that it's unlikely that those test substances actually are pure talc.
BY MS. APPEL:
Q. So again, Dr. Carson, in forming your opinions, you have done so on the belief that all the talc powder products or just pure talc do, in fact, contain asbestos?
MS. O'DELL: Objection to form.
A. It is my opinion that all talcum powder products do contain a certain amount of asbestos, even if it's extremely small.
My opinions have been formed

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based on research that has been done on available talcum powder products, so I guess the research would have been done using some small quantity of asbestos in all of those studies.
BY MS. APPEL:
Q. You also testified today, Dr. Carson, that you have found in your research that there is a dose-response relationship between talcum powder products and ovarian cancer, correct?
A. Well, a number of the research studies, the epidemiology studies have shown positive and statistically significant trends.
Q. And those trends that you're relying on, Dr. Carson, actually only relate to duration and frequency, correct?
MS. O'DELL: Objection to form.
A. Yes, they do relate to duration and frequency, which is the only surrogate we have for dose.
BY MS. APPEL:
Q. So in forming your opinion,

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Dr. Carson, you have not determined a level of harmful exposure to talcum powder products that causes ovarian cancer?
A. That's correct.
Q. And you did not conduct a dose assessment between talcum powder products and ovarian cancer, correct?
MS. O'DELL: Objection to form.
A. Well, I did not conduct a dose-response, but I am of the opinion that there's no safe threshold for exposure to a carcinogen until such a threshold is identified.
BY MS. APPEL:
Q. And does that include Category 2B particles as well --
MS. O'DELL: Objection.
BY MS. APPEL:
Q. -- that it's a possible carcinogen?
MS. O'DELL: Objection to form.
A. It includes the talc that was discussed in the IARC report. Those conclusions have nothing to do with how it's

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classified by IARC.
BY MS. APPEL:
Q. But it's your opinion that a possible carcinogen -- strike that.
It's your opinion that any dose of a possible carcinogen can cause cancer?
MS. O'DELL: Objection to form.
A. Yes, I think there is a potential for any dose of a carcinogen to cause a cancer. There's also the principle that the lower the dose, the less likely it is, the lower the risk is for developing a cancer.
BY MS. APPEL:
Q. And your opinion extends to those particles that have not been identified as carcinogens, but may just be possible carcinogens?
A. I think talc has been identified as a carcinogen.
Q. So you disagree with the IARC classification?
A. The IARC 2B classification is a carcinogenic classification.

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Q. But you recognize and -- that there are different types of categories that IARC has?
A. Yes.
Q. And that -- it's that talc that does not contain asbestos was not, in fact, categorized as a Group 1, correct?
A. That's correct.
Q. So is it your opinion, then, looking at other 2B-classified particles by IARC, that any exposure to pickled vegetables would cause cancer?
A. We know that there are a number of carcinogens that are regularly present in things like the food that we eat. We have a rule that says that those things should not be included in food items unless they have passed a particular exemption process.
Pickled vegetables are something that people have been familiar with and have been using for hundreds of years, and things like talcum powder are things that have been used for -- well, at least a hundred years, but probably considerably

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longer.
And whether or not those things are carcinogens, there are people who still find enough value to offset that factor in their own lives and they can make their own decisions regarding their exposure.
It's a similar concept to people who choose to smoke. Although smoking is an addictive behavior, people are aware that it causes disease, including cancer, and yet they continue to smoke.
We continue to eat grilled meats, even -- most of us know now that grilled meats contain polycyclic aromatic hydrocarbons that are known carcinogens, some of them Group 1 carcinogens, and yet, we continue that practice and revel in it even. That's just part of what we do as human beings.
The issue with talc is a complicated question in my mind. I think I'm straying a bit from your -- from your question, but baby powder, for example, is something that has a very -- very dear sort

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of relationship to many people.
The experience with that from the time you were a baby until you grow up and have your own children involves a lot of the use of baby powder in many, many households. That's a difficult relationship to break. It's psychological as much as it is knowledge based.
So as we go through the decades, we get a little safer and safer as we begin to peel these habits, these dangerous habits away from our lives and accept better lifestyles.
MR. ZELLERS: Move to strike as nonresponsive.
MS. APPEL: Respectfully --
MS. BOCKUS: Is he finished?
MR. ZELLERS: I don't think so.
THE WITNESS: I can go on.
BY MS. APPEL:
Q. Yeah. My question was more narrow, and I was analogizing your opinion as to talcum powder and was asking about other 2B classifications, and my example --

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A. Pickled vegetables.
Q. -- I had was pickled vegetables, and the question was whether or not is your opinion that any consumption of pickled vegetables causes cancer?
MS. O'DELL: Objection to form.
A. I believe the primary form of cancer that's potentially related with pickled vegetables is stomach cancer, and there is a slight increase in risk with consumption of pickled vegetables for everybody who does it.
BY MS. APPEL:
Q. Okay. And what about gasoline or exhaust?
A. Gasoline meaning the fuel?
Q. Yes.
A. Well, gasoline used to contain a significant amount of benzene, which was a -- determined to be a carcinogenic substance. In recent years, most of the benzene has been removed from gasoline, so now there's very little benzene in vapors that are expressed.

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But there's a small amount. So when you inhale gasoline vapors, you are also exposing yourself to a very small amount of a carcinogenic substance.
As far as exhaust is concerned, diesel exhaust in particular has -- contains particles that have been identified through various bioassays to be carcinogenic. So diesel exhaust is regulated as a carcinogenic material, even though we continue to be exposed.
Q. And it's your opinion that any exposure that we all incur related to exhaust will cause us cancer?
MS. O'DELL: Objection to form.
A. It will cause an increase in risk of cancer. Doesn't necessarily cause cancer in everybody.
BY MS. APPEL:
Q. Okay. Are you aware that Saed has been hired by plaintiffs' counsel in this litigation?
A. I am. And when I misspoke earlier today regarding the Taher paper, I

was thinking of the Saed paper.
Q. Okay. Last question: Counsel was asking you about the migration process, and you mentioned that in the course of particles moving up the track, that some of it may come back out even after it reaches the fluid surrounding the ovaries, correct?
A. Yes.
Q. So if particles have the ability to come back out, that means that there is, in fact, some form of an intrinsic elimination system.
A. Well, if this is all based on mass action, it would not necessarily be an intrinsic elimination system, and I believe that talc particles, once they produce an inflammatory response, they become sequestered within that inflammatory milieu and no longer are available for movement back out into the fluid.
I'm sure there's some small percentage of them that are an exception to that, but for the majority, that would be the case.



MS. APPEL: Okay. That's all I have. Thank you, Dr. Carson.
MS. TINSLEY: I don't have any questions.
MS. O'DELL: Okay. Why don't we take a short break.
THE VIDEOGRAPHER: Off the record at 5:37, end of Tape 4.
(Recess taken, 5:37 p.m. to 5:44 p.m.)
THE VIDEOGRAPHER: We're on the record at 5:44, beginning of Tape 5.
MS. O'DELL: Dr. Carson, I don't have any questions, so this will conclude your deposition.
MR. ZELLERS: Thank you, Doctor.
THE VIDEOGRAPHER: Going off the record, 5:44. End of deposition, end of Tape 5.
(Proceedings recessed at 5:45 p.m.)
--o0o--



CERTIFICATE

I, MICHAEL E. MILLER, Fellow of the Academy of Professional Reporters, Registered Diplomate Reporter, Certified Realtime Reporter, Certified Court Reporter and Notary Public, do hereby certify that prior to the commencement of the examination, ARCH I. "CHIP" CARSON, M.D., Ph.D. was duly sworn by me to testify to the truth, the whole truth and nothing but the truth.

I DO FURTHER CERTIFY that the foregoing is a verbatim transcript of the testimony as taken stenographically by and before me at the time, place and on the date hereinbefore set forth, to the best of my ability.

I DO FURTHER CERTIFY that pursuant to FRCP Rule 30, signature of the witness was not requested by the witness or other party before the conclusion of the deposition.

I DO FURTHER CERTIFY that I am neither a relative nor employee nor attorney nor counsel of any of the parties to this action, and that I am neither a relative nor employee of such attorney or counsel, and that I am not financially interested in the action.

_____

MICHAEL E. MILLER, FAPR, RDR, CRR
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Notary Public in and for the
State of Texas
My Commission Expires: 7/9/2020

Dated: January 22, 2019



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ACKNOWLEDGMENT OF DEPONENT

I, ARCH I. "CHIP" CARSON, M.D., Ph.D., do hereby certify that I have read the foregoing pages and that the same is a correct transcription of the answers given by me to the questions therein propounded, except for the corrections or changes in form or substance, if any, noted in the attached Errata Sheet.

_____

ARCH I. "CHIP" CARSON, M.D., Ph.D. DATE

Subscribed and sworn to before me this _____ day of _____, 20 _____.

My commission expires: _____

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Notary Public



LAWYER'S NOTES

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**F**

## I

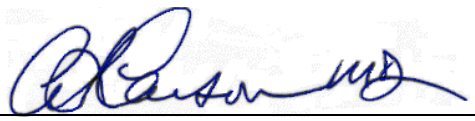
# Exhibit 5

**UNITED STATES DISTRICT COURT**
**DISTRICT OF NEW JERSEY**

| | |
|---|---|
| **IN RE JOHNSON & JOHNSON TALCUM POWDER PRODUCTS MARKETING, SALES PRACTICES, AND PRODUCTS LIABILITY LITIGATION**<br><br>***THIS DOCUMENT RELATES TO ALL CASES*** | **MDL NO. 16-2738 (FLW) (LHG)** |

# RULE 26 EXPERT REPORT OF ARCH CARSON, MD, PHD

Date: November 16, 2018



Arch Carson, MD, PhD

**Talcum Powder and Ovarian Cancer**

1. Introduction

I was asked to explain the relationship between the regular perineal use of talc-based personal hygiene products and the subsequent development of ovarian cancer in their users. I intend this report to explain this relationship. I will describe ovarian cancer, what is known about its natural history, and will present statistics regarding its incidence, prevalence and fatality. I will then describe what talc is and why talcum powder is used in personal care products. I will then present the scientific evidence linking talc-based personal hygiene products and their components with cancer, and will show how the various components of this evidence, along with other data, lead me to conclude that regular perineal application of talcum powder products causes ovarian cancer in some users, and raises the risk of ovarian cancer in all users.

2. Qualifications

I am a physician who specializes in the practice of medical toxicology. I am currently an Associate Professor at the University of Texas School of Public Health in Houston and the Program Director of the Occupational and Environmental Medicine Residency training program at the University of Texas Health Science Center at Houston. I received my medical degree from the Ohio State University and a doctor of philosophy degree in Toxicology from the Kettering Laboratory at the University of Cincinnati. I am board certified by the American Board of Preventive Medicine in Occupational Medicine, and have been in the continuous practice of medical toxicology since 1991. My professional activities have included patient care, basic and applied research, teaching of medical students, graduate students and post-graduate medical trainees, and professional consulting. I have been a program director of the NIOSH-funded Education and Research Center at the University of Texas for 19 of the last 21 years. Other major collaborations include as Liaison for the World Health Organization Collaborating Centre in Occupational Health and as environmental exposure consultant to the MD Anderson Cancer Center in Houston. My curriculum vitae is attached to this report as Exhibit A.

3. Information reviewed and methodology employed

In the preparation of this report, I have reviewed relevant published scientific and medical literature, reports and documents produced in the process of litigation, and various other documents and websites that I believed to be pertinent to the refinement or extension of my professional opinions. I applied the same methodology and scientific rigor in this research that I use in my academic and clinical practice. Documents and other sources which I considered in reaching my opinions are listed in Exhibit B, “Materials and Data Considered.”

4. What is ovarian cancer?
    a. What is cancer?

    All types of cancer involve the uncontrolled growth and accumulation or dissemination of cells that originated from normal cells, but have been altered so that they behave differently. The many cells of a single cancer that result from this change are typically all derived from a single progenitor cell, and represent a clone of cells. When this clone

reaches sufficient numbers, the cells themselves may develop into a recognizable "mass" that is called a tumor. Tumors may cause symptoms and other health problems simply by taking up space and putting pressure on neighboring structures or blocking important fluid channels or nerves, thus disrupting normal functions of the body. Still other cancers can proliferate into the blood stream. As the number of cancerous cells increase, the biochemically active substances that they produce can also become a problem resulting in abnormal biological responses throughout the body. Some substances that might become a problem in this way include normal or abnormal hormones, enzymes, antibodies, and proteins. Cancerous cells are considered malignant if they lose their normal tendency to stop proliferating when they have filled a space or the bounds of their particular tissue type, referred to as contact inhibition. Malignant cells ignore these boundary cues and may invade other tissue spaces and organs with devastating results. They may also migrate via the blood stream or other routes to distant sites within the body where they set up a new location of tumor growth and tissue invasion. This process is called metastasis. Typically, cancers are not diagnosed until they produce sufficient symptoms or biochemical abnormalities that lead to an exhaustive diagnostic search resulting in their discovery. Occasionally, cancers are discovered accidentally as part of another investigation, e.g. a chest x-ray may find an asymptomatic lung cancer; a blood test may disclose a telltale abnormality. Still fewer cancers are discovered before they cause health problems through screening tests that are sensitive and specific enough to detect common cancers at a preclinical and hopefully highly treatable stage, e.g. routine colonoscopies to detect colon cancer, or PSA blood tests to detect prostate cancer.

b. Carcinogenesis-a two-step process

The process of normal cells becoming cancer cells is generally recognized as resulting from a two-step process.

**Initiation**. During initiation, a change is produced at one or more places in the DNA of a cell's chromosomes. Because the DNA represents the genetic code that becomes duplicated and passed along to cells that arise from it, when that cell divides to produce two cells, the change to the genetic code is also duplicated and is present in both of them.

Normally, the abnormal cell that results from a change in the genetic code cannot survive because its cellular machinery is also abnormal and poorly or non-functional. Less often, if the cell is able to survive in the body, it is still abnormal and deformed, and is recognized by the body's immune system as alien. The immune system attacks it and destroys it, and it does not survive. In the very rare instance that an alteration to the genetic material results in a survivable hereditary change that is not fatal, and which can escape the surveillance of the body's immune system, the resulting clone may live and persist. (Coussens LM, 2002)

**Promotion** - Once a cancer clone has been produced, it is at risk for being discovered and destroyed by the body's immune system, or failing to thrive in an environment for which it is not suited. Promotion is the process by which the cancer clone is shielded

from the body's defenses and is stimulated to undergo rapid growth, transforming a microscopic cancer clone into a self-sustaining symptomatic cancer over time. (Ferrante D, 2007) (Coussens LM, 2002)

Most known carcinogenesis events occur by the two-step process and involve a long latent period between the moment of the alteration in the genetic material and the recognition that a cancer is present. In human cancers, this latent period is often several months to many years in length. The latency period for ovarian cancer, generally, and for cancers induced by environmental agents is usually quite long, often >20 years. (Nadler DL, 2014) Promotion occurs throughout the latent period and stimulates the growing cancerous cells to become a recognizable cancer. A third stage in the natural history of a cancer, referred to as Progression, involves maturation, differentiation or de-differentiation and accumulation of transcriptional changes that solidify the tumor's growth rate and invasiveness. Some carcinogenic substances are initiators and some are promotors, and still others are called complete carcinogens because they are capable of initiation and promotion.

c. Ovarian cancer

Ovarian cancer is a group of cancers that arise in the ovary or in adjacent tissues. It is estimated that about 22,240 women will receive a new diagnosis of ovarian cancer and about 14,070 women will die from ovarian cancer in the United States in 2018. (American Cancer Society, n.d.) (Torre LA, 2018) Ovarian cancer ranks fifth in cancer deaths among women, and first due to cancers of the female reproductive system. Most ovarian cancers are not discovered until they have reached an advanced stage and have spread to sites elsewhere in the body. Because advanced ovarian cancers are more difficult to treat, they have a high fatality rate. For these reasons, any effective prevention of ovarian cancer or reduction in ovarian cancer risk can have a significant impact on this disease and can save many women's lives.

There are several recognized forms of ovarian cancer that are distinguished by the specific tissues from which they arise, or the microscopic characteristics of the tumor cells themselves. About 85% to 90% of malignant ovarian cancers are epithelial ovarian carcinomas, and the majority of these are of the serous type (American Cancer Society, n.d.) (Prat, 2015). Ovarian, fallopian tube, and peritoneal cancers have a similar clinical presentation and are treated similarly, and current evidence suggests that they may have a common origin, supporting a common staging system (Soong TR, 2018).

Despite significant advances in cancer diagnosis and therapies over the past several decades, there have been few changes in the incidence or fatality rates for ovarian cancer. Consequently, it is worth considering preventable environmental causes of the ovarian cancer epidemic. (Woodruff, 1979) (LA Torre, 2018)

5. What is talc?
    a. General

Talc is a hydrated magnesium silicate mineral produced through a metamorphic geological process and having the generalized chemical formula $Mg_3Si_4O_{10}(OH)_2$. Some substitution of atoms occurs in variations of talc found in nature. Small amounts of Aluminum (Al) or Titanium (Ti) can substitute for Silicon, and small amounts of Iron (Fe), Manganese (Mn), Aluminum (Al) and Calcium (Ca) can substitute for Magnesium. This produces slight variations in the color, hardness and chemical properties of the mineral. Talc is the softest mineral on the Mohs Hardness Scale. (King, n.d.) It is essentially insoluble in water, but is slightly soluble in dilute mineral acids. The process seems to involve the extraction of magnesium and other cations leaving only the silicate as silicic acid and silica.

The commercial value of talc stems from its crystalline structure. Most talc is present in natural deposits as the platy form of talc, in which the talc crystals are arrange in large flat sheets running parallel to one another. These sheets are attracted to each other by weak Van der Waals forces that can be easily overcome by mechanical forces, causing the sheets to slide on each other. On the macro scale, this property gives talc its characteristic slippery feeling on the skin. The platy structure also gives talc its ability to absorb moisture and oil. Some talc is found as a fibrous crystalline structure, similar to some asbestos, also a magnesium silicate mineral. In fact, these two minerals are closely related in terms of their formation and composition. Talc deposits are often intermingled with asbestos and vice versa. (Rohl, 1974) (Rohl AN, 1976) (National Institute for Occupational Safety and Health, 2011) (Lockey, 1981)

b. Talcum Powder and Cancer.

Numerous studies have examined the cancer causing characteristics of talc. (Wild, 2006) Talc has caused cancer when implanted in various tissues and under the skin in laboratory animals. It causes inflammation and fibrotic reaction, including the chemotaxis of inflammatory immune cells, and accelerated growth and division of cells in the involved tissues (Okada, 2007). This is a normal body process that leads to the thwarting of infection and rapid healing, but in the absence of tissue injury, accelerated growth and cell division has the effect of amplifying and propagating viable genetic mutations, leading to cancer. Talc particles have been repeatedly demonstrated in ovarian tumor tissues (Henderson WJ C. J., 1971) (Henderson WJ T. H., 1979) and in inflammatory tissue in otherwise normal ovaries (Mostafa SAM, 1985). In 2006, the International Agency for Research on Cancer (IARC) evaluated the published evidence for the carcinogenicity of talc, not containing asbestiform fibers, when inhaled into the respiratory system and when applied to the perineum in personal hygiene activities. The agency concluded that talcum powder is a “possible human carcinogen” (Group 2B) when applied to the perineum, meaning that there is insufficient evidence of carcinogenesis in humans, but strong evidence in other mammalian species. IARC also concluded that there was insufficient evidence of carcinogenicity by the inhalation route (Group 3). (International Agency for Research on Cancer, 2010) Since that time,

numerous other studies have added to the data on this issue. A recent meta-analysis showed that talc workers do have an excess of lung cancers. (Chang C-J, 2017)

When implanted under the skin or into tissues of laboratory animals, talcum powder induces an inflammatory response. This reaction involves the chemotaxis of inflammatory cells of the immune system, lymphocytes, neutrophils and macrophages, the release of cytokines that promote membrane permeability and stimulate cell division. As this reaction matures over time, granulomas may begin to develop. All of this signifies that talcum powder is an effective and potent promotor of already initiated genetic alterations. (Fletcher NM M. I., 2018) (Fletcher NM S. G., 2018) (Saed GM, 2017) (Radić I, 1988) (Okada, 2007) Other studies have demonstrated the ability of these same reactions to satisfy the carcinogenic initiation step, characterizing talcum powder as a complete carcinogen. (Shukla A, 2009) (Fletcher NM M. I., 2018)

c. What about asbestos and other components in talc and talc-based products?

Talcum powder products in the marketplace have been shown to contain asbestos. (Paoletti L, 1984) (VanOrden D, 2000) (VanGosen BS, 2004) (Longo WE, 2017) Asbestos is conclusively recognized as a cause of ovarian cancers. The IARC Working Group concluded that "a causal association between exposure to asbestos and cancer of the ovary was clearly established, based on five strongly positive cohort mortality studies of women with heavy occupational exposure to asbestos, (International Agency for Research on Cancer, 2012)" and "studies showing that women and girls with environmental, but not occupational exposure to asbestos had positive, though non-significant, increases in both ovarian cancer incidence and mortality. (Acheson ED, 1982) (Fox, 1982) (Berry G, 2000) (Newhouse ML, 1972) (Reid A H. J., 2008) (Reid A S. A., 2009) (Pira E, 2005) (Magnani C, 2008) (Bertolotti M, 2008) (Ferrante D, 2007) (Germani D, 1999) (Rösler JA, 1994) The classification determined by IARC included all forms of asbestos and talc containing asbestiform fibers (fibrous talc). I have seen evidence that Johnson & Johnson's talcum powder products contain asbestos and fibrous talc. [1]

d. Carcinogenic metals in talcum powder

In addition to other related minerals, talcum powder may contain varying amounts of chromium, cobalt and nickel, metal ions that are recognized as cancer causing. These ions leach out of the talcum powder slowly over time, resulting in continuous, low-level exposure of the surrounding tissues to carcinogenic metals. (Jurinski JB, 2001) I have seen evidence that Johnson & Johnson's talcum powder products contain nickel (Group 1

[1] Ex. 28, Hopkins Dep. (Aug. 16 & 17, 2018; Oct. 26, 2018; and Nov. 5, 2018); Ex. 47, Pier Dep. (Sept. 12 & 13, 2018); Expert Report of William E. Longo, PhD and Mark W. Rigler, PhD (Nov. 14, 2018)

human carcinogen), chromium (Group 1 human carcinogen), and cobalt (Group 2B-possible human carcinogen).[2]

e. Other potentially cancer-causing constituents

Johnson & Johnson's Baby Powder and Shower to Shower contain numerous ingredients that have been added to the products, i.e. fragrance chemicals, some of which have been shown to produce cancer in laboratory animals. These substances are likely to be present in very small or trace quantities, and likely present a lower level of risk than the major components, by mass. Nonetheless, any additional risks are added as part of a total risk profile. I have reviewed the report of Dr. Michael Crowley and agree with his conclusions that these chemicals may contribute to the inflammatory properties, toxicity, and potential carcinogenicity of the products.[3]

6. Epidemiology linking talcum powder and ovarian cancer

Many research studies have shown a strong association between talcum powder exposure and the development of ovarian cancer. (Langseth H, 2008) (Terry KL, 2013) (Schildkraut JM, 2016) (Trabert, 2016) (Berge W, 2017) (Cramer Daniel W, 2016) (Penninkilampi R, 2018)

a. What evidence links exposure to talcum powder products with ovarian cancer?

Multiple epidemiological studies have examined the link between the personal hygiene use of talc containing products and the occurrence of ovarian cancers (Booth M, 1989) (Cook LS K. M., 1997) (Cook LS e. a., 1997) (Cramer DW, 1982) (Whittemore AS, 1988) (Harlow BL W. B., 1989) (Chen Y, 1992) (Harlow BL C. D., 1992) (Rosenblatt KA, 1992) (Hartge P, 1988) (Tzonou A, 1993) (Chang S, 1997) (Heller DS, 1996) (Penninkilampi R, 2018). Talcum powder causes proliferation of human (Prat, 2015) ovarian cells in culture (Buz'Zard AR, 2007), and causes these cells to express reactive oxygen species (ROS) (Buz'Zard AR, 2007).

The research investigating the link between talcum powder exposure and ovarian cancer has been reviewed as a scientific whole at multiple stages. (Harlow BL H. P., 1995) (Ness Roberta B, 1999) (Muscat JE, 2008) (Terry KL, 2013) (Berge W, 2017) (Penninkilampi R, 2018)

Laboratory, animal and human studies support the conclusions that talc causes ovarian cancer, and have filled in the blanks that establish biological plausibility and scientific coherence. (Jaiswal M, 2000) (Balkwill Fran, 2001) (Okada, 2007) (Saed Ghassan M, 2017) (Harper, 2019)

7. Talcum powder product use

[2] Ex. 47, Pier Dep. (Sept. 12 & 13, 2018)

[3] Expert Report of Michael Crowley, PhD (Nov. 12, 2018).

Numerous studies have interviewed women regarding their personal practices of application of talc-based powders to the perineal area. Due to variations in these practices, it has been difficult to estimate dose in order to evaluate the dose response relationship for ovarian cancer. It is also difficult to exactly estimate the quantity of talcum powder administration during personal hygiene activities. For studies that attempted to determine amount of exposure, most relied on a method of estimating the frequency of application and/or the duration of those practices, then simply multiplying to reach a total number of applications over time. (Harlow BL H. P., 1995) (Langseth H, 2008) A review of studies of perineal talcum powder or cornstarch application suggests that the use of cornstarch instead of talcum powder reduces the risk of ovarian cancer. (Whysner J, 2000)

8. Other evidence
    a. Transport of talc-containing materials from the perineum to the upper reproductive tract and body cavities has been shown to occur with startling regularity and with respect to a wide variety of particulate materials. (Egli GE, 1961) (Venter PF, 1979) (Blumenkrantz MJ, 1981) (Halme J, 1984) (Sjösten ACE, 2004) Clearly, sufficient particulate materials applied routinely to the perineum have ready access and in sufficient quantities to produce biological responses in internal tissues, including the ovaries and surrounding structures. There are a limited number of animal studies suggesting that this transport does not occur. (National Toxicology Program, 1993) These are not as compelling as the human evidence because of anatomical and physiological differences between animals and humans in this regard, as well as the overwhelming evidence in humans.

9. Conclusions and opinions

The following conclusions and opinions are expressed with respect to reasonable medical and scientific certainty and I have applied reliable scientific principles and methods to the facts in reaching them. These opinions are based upon the documents and literature reviewed and cited herein, and also upon my own professional training and experience in practice of medicine and medical toxicology.

## I. Talcum powder products sold for personal hygiene use are carcinogenic.

Talcum powder is immunogenic, producing chronic inflammation in the tissues in which it sequesters, with the attraction of lymphocytes and macrophages and the ongoing local release of pro-inflammatory cytokines and reactive oxygen species. Further, all talcum powder has some component of mineral fibers that are toxic to macrophages and intensify the inflammatory response and stimulate cell growth and proliferation. The presence of asbestos, fibrous talc, carcinogenic metals and other chemicals further intensify this effect. Cohort and case-control studies have shown statistically significant associations between talc-based powder use and ovarian cancers. The presence of carcinogenic metals such as, chromium, cobalt and nickel, and toxic fragrance components in commercial talcum powder products, adds to their carcinogenic potency. Talcum powder is a complete carcinogen and can both initiate and promote the development of cancers in the tissues in which it sequesters.

## II. Perineal use of talcum powder products for feminine hygiene purposes results in direct exposure to the female reproductive tract.

A proportion of talcum powder from personal hygiene applications to the perineum is transported or migrates through the reproductive tract, through the patent fallopian tubes, onto the ovaries and into the pelvic cavity. Talc particles have been identified in reproductive system structures of women who utilize talc powders. These include the uterine cervix, the endometrium, the fallopian tubes and the ovaries. Inhalation is likely a secondary route of exposure.

## III. Common carcinogenic constituents of talcum powder products participate in and add to the carcinogenic process.

Naturally occurring carcinogenic components of talcum powder, i.e. asbestos, chromium, nickel, and cobalt, are liberated in bodily fluids and tissues and are free to exert their carcinogenic effects. Added substances that are toxic or carcinogenic, i.e. fragrance chemicals, may also contribute to these effects. This process is the most intense where the duration is the longest. Because the ovaries have no intrinsic elimination system, the transport of talc particles and their constituents reaches the ovaries where it stalls and sequesters. For these reasons, ovarian tissue is most at risk for the carcinogenic effect of these substances.

## IV. Regular perineal application of talcum powder products causes epithelial ovarian cancer in some users, and raises the risk of ovarian cancer in all users.

Multiple case-control and cohort epidemiological studies have looked at the relationship between the perineal use of talc-based powders and the eventual development of epithelial ovarian cancer. Most, but not all, of these studies show a consistent positive relationship. When confounding and bias are exhaustively considered, the positive association remains. I conclude that the apparent cause and effect relationship between perineal talcum powder use and ovarian cancer is real, amounting to about a 30% increased risk of ovarian cancer in talcum powder product users. At the current rate of ovarian cancer diagnosis and mortality, elimination of this source of risk could result in over 3,000 lives saved in the U.S. each year.

In 1965, Sir Austin Bradford Hill published what has come to be recognized as the best collection of factors to consider for the assessment of scientific evidence that relates the causation of disease to environmental exposures (Hill, 1965). These factors include: (1) Strength of association, (2) Consistency of the evidence, (3) Specificity, (4) Temporality, (5) Biological gradient, (6) Plausibility, (7) Coherence, (8) Experiment, and (9) Analogy. Below I provide my evaluation of the scientific evidence with respect to the Hill factors.

**Strength of association** –Many epidemiological studies have attempted to examine the association between perineal use of talcum powder products and ovarian cancer. Most of these have been case-control studies, where women diagnosed with ovarian cancer are paired with others of similar demographic background who do not have ovarian cancer. All of these women are interviewed about their past practices and exposures, including the use of talcum powder products. The resulting data are analyzed to compute an odds ratio (OR) that describes the

likelihood of those with cancer having had greater exposure to talcum powder than those who did not. Cohort studies selected populations of women, assessing them for many factors, including perineal talcum powder use, and followed them over time counting the occurrences of ovarian cancers. These studies were than able to compute a relative risk (RR) of exposure to talcum powder resulting in ovarian cancers. Of more than 25 case-control studies in the literature, the heavy majority showed positive and significant ORs for perineal talcum powder use and ovarian cancer. The three cohort studies did not find a significant relative risk of perineal talcum powder exposure leading to ovarian cancer, but did show positive non-significant trends. Several research groups have looked at the totality of the research evidence, evaluated the published study reports, and have reanalyzed those data on a common playing field through meta-analyses. Taken in their totality, and accounting for sources of bias and differing statistical treatments, these epidemiological studies support a strong association between the perineal use of talcum powder and ovarian cancer.

**Consistency of the evidence** – As stated above, the majority of epidemiological studies that have investigated the link between perineal talcum powder use and ovarian cancer have reported positive associations. These studies are consistent in their findings of a relationship between perineal use of talcum powder products and the development of ovarian cancer. Further, recent meta-analyses of previously published studies have verified the comparability of the research methods used and the consensus of conclusions.

**Specificity** – Specificity is the concept that a specific disease, rather than a host of diseases, is produced by a particular exposure, and that the exposure is a principal cause of the disease. Although talcum powder is known to cause non-specific inflammation in many tissues where its residues locate, the stimulation of ovarian cancer is particularly associated with the presence of talc in the ovaries and fallopian tubes. Of known factors associated with ovarian cancer, i.e. nulliparous state, early menarche, late menopause, oral contraceptive use, living in the twentieth century and beyond, perineal talcum powder exposure is proving to be prominent among them.

**Temporality** – If a particular exposure is the cause of a particular disease, then the onset of exposure should precede the onset of the disease. Studies investigating the link between perineal talcum powder exposure and ovarian cancer are designed to compare those with prior exposure to those who are not exposed, and so the scientific evidence supports this consideration.

**Biological gradient** – A basic toxicological principle is that a greater exposure intensity will result in a larger proportion of those exposed expressing the toxic effect, in this case ovarian cancer. In order to determine the intensity of a long-term environmental exposure, typically a measure of frequency or quantity of use is multiplied by the duration of such use. This allows categorization of exposure levels and comparisons. Although some studies have failed to find evidence of a dose-response relationship, several more recent reports have shown a clear dose-response when the number of subjects rose to a level producing sufficient statistical power to allow the analysis after subdivision of subjects into pertinent categorical groups, and frequency and duration were measured (Schildkraut JM, 2016) (Cramer Daniel W, 2016) (Wu, et al., 2009).

**Plausibility** – This factor expects the rational presentation of a mechanism whereby the exposure in question leads to the disease. Thus, if no such mechanism can be proposed, it is less likely that causation will be supported. In the case of ovarian cancer, the mechanism supported in the literature is as follows: Talcum powder products are applied to the perineal area in the course of routine personal hygiene practices. This element is supported by the existence of these products in the marketplace for many years and the statements of subjects interviewed for the purpose of conducting the scientific research discussed elsewhere in this report. Portions of the applied powders are transferred via active processes or passive mass action movements into the female reproductive tract, some making it all the way to the distal fallopian tubes, the ovary surfaces and the pelvic and peritoneal cavities. This element is supported by the observations that particulate materials of differing variety can make their ways along these pathways to the listed destinations, and the finding and confirmation of talc particles in normal ovarian tissues and ovarian tumor tissues at the time of oophorectomy or autopsy. Once reaching the target tissues, talcum powder and its constituents initiate carcinogenesis via multiple means, including, inflammation with chemotaxis of inflammatory cells, liberation of cytokines, and reactive oxygen species, inactivation of TP53 genetic modulator, inhibition of DNA repair, and long-term promotion of genetic mutations via continuous inflammation and cellular growth stimulation.

**Coherence** – The proposed cause and effect relationship should not "seriously conflict with the generally known facts of the natural history and biology of the disease."(Hill, 1965) The proposal that talcum powder product use results in the occurrence of ovarian cancer is entirely consistent with what is known about other factors related to ovarian cancer, i.e. early menarche, late menopause, pregnancies, breastfeeding history, oral contraceptive use, etc. All are factors that influence the local inflammatory environment of the ovary and its surroundings and have the potential to promote existing transcriptional errors and mutations.

**Experiment** – Interventions, such as tubal ligation that decreases the incidence of ovarian cancer by blocking the exposure route, offers experimental support for this mechanism. The use of cornstarch-based dusting powders as a substitute for talcum powder products offers additional experimental support.

**Analogy** – Have there been other environmental exposures that have been associated with ovarian cancers that act via similar mechanisms? Talcum powder is somewhat unique in terms of its delivery mechanism. But beyond that, the case of asbestos exposure is similar. Asbestos exposure has resulted in excesses of ovarian cancers in exposed women, although the route of exposure is thought to be by inhalation. Nonetheless, asbestos is a mineral very similar both chemically and structurally to talc that has been found in the ovary and peritoneal cavity of exposed women. The mechanisms of carcinogenesis for both asbestos and talc are similar and analogous. Further, talc-based products contain asbestos and non-asbestos mineral fibers having carcinogenic potential.

When considering these factors, I gave the most weight to the compelling strength of association and consistency, as well as the well-described biologic mechanism.

The currently available scientific research, when considered in its totality, demonstrates a cause and effect relationship between the use of talcum powder products and the development of epithelial ovarian cancer. This opinion is reinforced by my consideration of the Hill factors for the assessment of causation.

In reviewing the scientific and medical literature on talcum powder product use, I also performed a risk assessment and considered whether perineal use of those products poses a safety risk to consumers. This involved careful consideration of the epidemiological literature, data on the dose-response relationship and exposure, as well as the nature of these products, which are used primarily for personal care. I also considered evidence of the toxicity of these products, for which repeated testing and analyses have shown to contain carcinogens.

In considering the weight of this epidemiologic, toxicologic, and mechanistic evidence, across multiple studies, time, demographics, and researchers, demonstrating a consistent association between perineal use of talcum powder products and ovarian cancer, it is my opinion that talcum powder products increase the risk of ovarian cancer and pose a significant health hazard.

In conclusion, it is my opinion that the perineal use of talcum powder products causes ovarian cancer in some users and increases the risk of ovarian cancer in all users of these products.

All of my opinions in this report are provided with respect to a reasonable degree of medical and scientific certainty. I reserve the right to amend or supplement my report as new information becomes available.

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# Exhibit A

# Curriculum Vitae

Arch I Carson MD PhD

Occupational Medicine and Medical Toxicology

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**Biosketch**

Arch "Chip" Carson, MD, PhD is a physician (The Ohio State University), board certified in Occupational Medicine (American Board of Preventive Medicine), who holds a Doctor of Philosophy degree in Toxicology (University of Cincinnati, Kettering Laboratory). He has served on the faculty of the University of Cincinnati and the New York University Medical Center and joined the faculty of the University of Texas School of Public Health in 1992 in its Environmental Sciences Discipline and Occupational and Environmental Health and Aerospace Medicine Module. He is Associate Professor of Occupational Health, directs the Occupational and Environmental Medicine Residency Program and is a member of the research team of the Southwest Center for Occupational and Environmental Health, a NIOSH Education and Research Center, and WHO Collaborating Centre in Occupational Health. He maintains a clinical practice of occupational medicine and medical toxicology. In his more recent role as Medical Director for the University of Texas Medical Branch in Galveston, he is responsible for the health monitoring and care of more than 15,000 employees. He is a frequent consultant to governments, corporations and the legal community on matters related to industrial chemical exposure, toxicology and environmental justice. His research interests include: environmental and occupational chemical exposures, inhalation injuries, metal exposures and cancer, and professional training in occupational medicine.

**Professional Activities/Employment**

| | |
|---|---|
| 2017-18 | University of Texas Medical Branch, Galveston, Assistant Clinical Professor of Preventive Medicine and Family Medicine |
| 2017-18 | University of Texas Medical Branch, Galveston, Medical Director, Employee Health Services. |
| 2017-18 | Enbridge Corporation, Houston Texas, Medical Director, Employee Health Services. |
| 2010-18 | University of Texas Health Science Center, Houston, Associate Professor of Occupational Health. |
| 2010-18 | University of Texas Health Science Center at Houston, Program Director, Occupational and Environmental Medicine Residency. |
| 1991-18 | Private practice of Occupational Medicine and Toxicology, New York, Texas and Ohio. |
| 2011-18 | Spectra Energy Corporation, Houston Texas, Medical Director, Employee Health Services. |
| 1997-13 | Texas Medical Center Inc., Houston Texas, Medical Director, Employee Health Services. |
| 1992-08 | University of Texas School of Public Health, Assistant Professor of Occupational Medicine and Environmental Sciences. |
| 1998-08 | University of Texas Health Science Center at Houston, Program Director, Occupational and Environmental Medicine Residency. |
| 2003-08 | Southwest Center for Occupational and Environmental Health, Principal Investigator and Director, Diller Phosgene Exposure Incident Registry of the American Chemistry Council. |

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|---|---|
| 2000-06 | Chevron Phillips Chemical Company, Houston Texas, Corporate Medical Director. |
| 2003-05 | U.S. Department of Energy Office of Worker Advocacy Physician Review Panel Appointee. |
| 1997-04 | Southwest Center for Occupational and Environmental Health, Principal Investigator, City of Houston Lead Poisoning Epidemiology Project. |
| 1992-03 | UT Health Services, University of Texas Houston Health Science Center, Attending Physician, Occupational Medicine and Toxicology. |
| 1997-01 | University of Houston Downtown, Medical Director, Student Health Service. |
| 1998-99 | University of Texas School of Public Health, Convener of the Occupational/Environmental Health and Aerospace Medicine Module. |
| 1992-97 | Respiratory Consultants of Houston, PA, Attending Physician, Occupational Medicine and Toxicology. |
| 1992-95 | Exxon Chemical Americas, Baytown Polymer Center and Basic Chemicals Technology, Baytown TX, Consultant Physician. |
| 1990-91 | New York University Medical Center, Bellevue Hospital, Tisch Hospital, and Manhattan VA Hospital, New York NY, Dept. of Medicine, Clinical Instructor. |
| 1982-90 | Chemical Information Services Inc, Cincinnati OH, Associate in Toxicology. |
| 1978-87 | University of Cincinnati College of Medicine, Cincinnati OH, Instructor and Lecturer, Adjunct Assistant Professor of Industrial Toxicology. |
| 1974-79 | University of Cincinnati College of Medicine, Kettering Laboratory, Cincinnati OH, Research Technologist in Occupational Medicine and Clinical Studies. |
| 1969-74 | Millstone Inc., Cincinnati OH, Design Engineer, environmental control systems. |

**Educational Background**

| | |
|---|---|
| 2002 | Certificate of Board Eligibility, Medical Toxicology, American Board of Preventive Medicine/American Board of Emergency Medicine |
| 1992 | Certificate of Training - Residency in Occupational Medicine University of Texas Health Science Center at Houston, School of Public Health, and Southwest Center for Occupational and Environmental Health, Houston TX, 1992. |
| 1991 | Certificate of Training - Postgraduate Internship in Internal Medicine, New York University Medical Center and Bellevue Hospital Center, New York NY. |
| 1990 | MD - Ohio State University College of Medicine, Columbus OH. |
| 1987 | PhD - Kettering Laboratory, University of Cincinnati College of Medicine, Cincinnati OH, awarded in the field of "Environmental Health – Toxicology." |
| 1973 | BS - University of Cincinnati College of Arts and Sciences Cincinnati OH. Awarded in "Biological Sciences with Concentration in Engineering." |
| 1969 | Rensselaer Polytechnic Institute, Troy NY. Management Engineering |
| 1968 | Villa Madonna College, Covington KY. Certificate in Contemporary Physics. |

**Fellowships**

| | |
|---|---|
| 2011-13 | UTHealth, Health Educators Fellowship, University of Texas Health Science Center at Houston. |

1983-85 American Lung Association Fellowship in Lung Research (Inhalation Toxicology), American Lung Association of Southwestern Ohio, Grant.

1981-82 Owens Corning Fiberglas, Graduate Research Fellowship in Combustion Toxicology.

1979-80 National Institute for Occupational Safety and Health, Centers for Disease Control, Doctoral Fellowship in Industrial Toxicology.

**Certifications**

2012 License to practice medicine, State of Ohio 35.098635

2010 Certified Healthy Homes Specialist – National Environmental Health Association.

2002 Board Eligibility, Medical Toxicology, American Board of Preventive Medicine/American Board of Emergency Medicine.

1994 Board Certification, Occupational Medicine, American Board of Preventive Medicine.

1992 License to practice medicine, State of Texas J2524.

1991 License to practice medicine, State of New York 186563.

1982 Emergency Hazard Response, Environmental and Industrial Chemical Accident Management, U.S. Environmental Protection Agency.

1979 Pulmonary Function Testing for Occupational Surveillance, NIOSH #003.

**Professional Community Service**

2013-18 University of Texas Health Science Center at Houston, Steering Committee on Interprofessional Collaboration

2013-18 University of Texas Health Science Center at Houston, Chemical Safety Committee.

1998-18 Association of Environmental and Occupational Clinics/ATSDR community resource on toxic exposures and health consequences, Federal Region VI.

1997-18 City of Houston Biological, Chemical and Radiation Emergency Preparedness Program. Medical Toxicology On-Call Advisor to the Houston Medical Strike Team.

1998-18 Association of Occupational and Environmental Medicine Residency Directors. Chairman 2005-2006

2010-18
1997-08 University of Texas Health Science Center at Houston, Graduate Medical Education Committee

2010-18
1994-08 University of Texas Health Science Center, Houston, Community/Press Resource and Speaker via Public Information Office, (Toxic Exposures and Environmental Health).

1996-18 American College of Occupational and Environmental Medicine, Council on Academic Affairs and Co-chair, Academic Section 2004-2006. Occupational Medicine Residency Directors Committee, Chair 2006-2007, Appointed Member, Taskforce on the Future of Occupational Medicine Education 2005-2007. Appointed Co-chair, Taskforce on the Future of Occupational Medicine Education 2013-2015.

1996-18 Texas College of Occupational and Environmental Medicine. Secretary/Treasurer-2004-5, President Elect-2005-6, President-2006-7, Past President 2007-8.

2003-12 Boy Scouts of America, Sam Houston Council, Registered Adult Leader and Merit Badge Counselor.

2005-08 University of Texas School of Public Health, Practice Council Co-chair

2003-05 U.S. Department of Energy Office of Worker Advocacy Physician Review Panel Appointee.

1996-00 American Public Health Association, Occupational Health Subcommittee

1994-96 Advisory Board, National Environmental Education and Training Center (NEETC), Curriculum Development Committee.

1981-85 Tri-State Air Committee Inc., Cincinnati OH, (voluntary air quality organization) Scientific Advisor, Elected to Board of Directors in 1982, President and Chairman 1984-85.

1981-85 American Lung Association of Southwestern Ohio, Cincinnati OH, (voluntary health organization) speakers bureau.

1982-83 City of Cincinnati, Appointment to Occupational Health Scientific Liaison Board (municipal advisory committee).

1981-83 Cincinnati Area Toxic Substances Coalition, Cincinnati OH, (coalition of business, voluntary, and labor organizations with interest in environmental toxic substance issues) Cofounder and Chairman.

1982-83 Ohio River Valley Committee on Occupational Safety and Health, Cincinnati OH, (organized labor coalition) Scientific Resource Committee.

1972-82 Walnut Hills-Evanston Medical Center, Cincinnati OH, (primary care center) Board of Directors.

**Professional Societies**

1991-18 American College of Occupational and Environmental Medicine.

1991-18 Texas College of Occupational and Environmental Medicine

2007-18 Texas Public Health Association.

2006-18 International Congress on Occupational Health.

2003-18 American College of Medical Toxicology.

2002-06 Society of Occupational and Environmental Health.

2001-06 American Conference of Governmental Industrial Hygienists.

1994-00 American Public Health Association.

1983-87 American Industrial Hygiene Association.

1983-87 Society of Toxicology.

1980-85 American Thoracic Society, Associate Member and Participant in Occupational and Environment Scientific Session.

**Publications**

Anderson F, **Carson A**, Whitehead L and Burau K Age, Race and Gender Spatiotemporal Disparities of COPD Emergency Room Visits in Houston, Texas. Occupational Diseases and Environmental Medicine. 3:1-9, 2015. http://dx.doi.org/10.4236/odem.2015.31001.

Anderson F, **Carson A**, Whitehead L and Burau K. Spatiotemporal Analysis of the Effect of Ozone and Fine Particulate on CVD Emergency Room Visits in Harris County, Texas. Open Journal of Air Pollution, 3:87-99, 2014. http://dx.doi.org/10.4236/ojap.2014.34009.

Calcote, JC, **Carson, A**, Peskin, MF, Emery, RJ. An assessment of post-disaster psychological stress in hazardous waste operations and emergency response (HAZWOPER) workers. Disaster Med Public Health Preparedness. 7:452-460, 2013. PMID 24274124.

Delclos GL, Tullis LA, **Carson A**. The services industry. In Occupational and Environmental Lung Diseases. Tarlo SM, Cullinan, Nemery B eds. 2010 pp.258-271. Wiley-Blackwell, West Sussex, UK.

Pugach S, Clarkson T, (**Carson A**). Prenatal mercury exposure and postnatal outcome: clinical case report and analysis. Clin Toxicol 47:366-370, 2009.

Pauluhn J, **Carson A**, Costa DL, Gordon T, Kodavanti U, Last JA, Matthay MA, Pinkerton KE and Sciuto AM. Workshop summary: phosgene-induced pulmonary toxicity revisited: appraisal of early and late markers of pulmonary injury from animal models with emphasis on human significance. Inhalation Toxicology. 19(10):789-810, 2007.

Delclos GL, Gimeno D, Arif AA, Burau KD, **Carson A**, Lusk C, Stock T, Symanski E, Whitehead LW, Zock JP, Benavides FG and Anto JM. Occupational risk factors and asthma among health care professionals, American Journal of Respiratory & Critical Care Medicine. 175(7):667-75, 2007.

Savely SM, **Carson A** and Delclos GL. "A survey of the implementation status of environmental management systems in U.S. colleges and universities" J Cleaner Production, 15(7) 650-659, 2007.

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Delclos GL, Arif AA, Aday L, **Carson A**, Lai D, Lusk C, Stock T, Symanski E, Whitehead LW, Benavides FG and Anto JM. Validation of an asthma questionnaire for use in healthcare workers. Occupational & Environmental Medicine. 63(3):173-9, 2006.

Delclos GL, Bright KA, **Carson A**, Felknor SA, Mackey TA, Morandi MT, Schulze LJH and Whitehead LW. "A global survey of occupational health competencies and curriculum" International Journal of Occupational and Environmental Health; 11:181-194, 2005.

Nooka A, Duonghi L, **Carson A**, Hassan M. Assessing Occupational Risk for Pancreatic Cancer by Chemical Exposures and Work History: A Case-Control study at MD Anderson Cancer Center. American Association for Cancer Research, Orlando. March, 2004.

Mitchell CS, Moline J, Avery AN, Baker D, Blessman JE, **Carson A**, Cosby O, Darcey D, Ducatman A, Emmett EA, Forst L, Gerr F, Gochfeld M, Guidotti TL, Harber P, Hu H, Hegmann KT, Kipen HM, Levin J, McGrail MP, Meyer JD, Mueller KL, Prince S, Rubin R, Schwerha JJ, Sprince NL, Taiwo O and Upfal M. In response to the 2002, vol. 22, no. 4 article entitled "The rise and fall of occupational medicine in the United States" [Letter] Am J Preventive Med. 23(4):307-9, 2002.

**Carson A** and Delclos GL. "The Respiratory System," in Modern Industrial Hygiene: Volume II – Biological Aspects, JL Perkins, ed. 2003, American Conference of Governmental Industrial Hygienists, Cincinnati.

**Carson A**, Colombo S and Alavi. A, City of Houston Childhood Lead Poisoning Prevention Program: Case Density and Impact Analysis, March 31, 2000, Technical Report (Principal Investigator).

Townsend MC, Lockey JE, Velez H, **Carson A**, Cowl CT, Delclos GL, Gerstenhaber BJ, Harber PI, Horvath EP, Jolly AT, Jones SH, Knackmuhs GG, Lindesmith LA, Markham TN, Raymond LW, Rosenberg DM, Sherson D, Smith DD, and Wintermeyer SF. ACOEM Position Statement – "Spirometry in the Occupational Setting" JOEM; 42: 228-245, 2000.

Bright K, Delclos G, **Carson A**, Felknor S, Mackey T, Morandi M, Schultz L and Whitehead L. A Global Study of Occupational Health Competencies and Curricula, Report to the World Health Organization, March, 2000, Southwest Center for Occupational and Environmental Health.

**Carson A**, Guevara E, Delclos GL, Murray KA, Burau KD, Morandi MT, Felknor SA, ("A Study of General Health of Workers of the Industrial Complex of Barrancabermeja") in [Compendium on Occupational Health in the Petroleum Industry of Colombia: Technical and Scientific Report of the "Occupational Health in the Petroleum Industry" Project], 1999 Pan American Health Organization (co-author).

**Carson A**, Hangoc V and Bahrainwala M, City of Houston Childhood Lead Poisoning Prevention Program: Case Density and Impact Analysis, June 30, 1999, Technical Report (Principal Investigator).

**Carson A**, Spears B, and Burau K, City of Houston Childhood Lead Poisoning Prevention Program: Case Density and Impact Analysis, June 30, 1998, Technical Report (Principal Investigator).

**Carson A**, Detry M, Spears B, and Burau K, City of Houston Childhood Lead Poisoning Prevention Program: Case Density and Impact Analysis, June 30, 1997, Technical Report (Principal Investigator).

Delclos GL and **Carson A**, "Acute Gaseous Exposures," in Occupational and Environmental Respiratory Diseases, P Harber, M Schenker, and J Balmes eds. 1995, Mosby Yearbook Pub., St. Louis.

**Carson A**, "Respiratory Effects of Exposure to Fresh Smokes from Pyrolytic Decomposition of Styrene Plastic in Rats." Doctoral Dissertation, University of Cincinnati Kettering Laboratory, 1987.

**Carson A**, "A Dynamic Method for the Generation of Fresh Smokes From Combustion or Pyrolytic Decomposition of Structural Materials." Doctoral Dissertation, University of Cincinnati Kettering Laboratory, 1987.

Samuels SJ, Lemasters GK and **Carson A**, "Statistical Methods for Describing Occupational Exposure Measurements," Am. Ind. Hyg. Assoc. J., 46:427-433, 1985.

Lemasters GK, **Carson A** and Samuels SJ, "Occupational Styrene Exposure for Twelve Product Categories in the Reinforced-Plastics Industry," Am. Ind. Hyg. Assoc. J., 46:434-441, 1985.

Lockey JE, Brooks SM, Jarabek AM, Khoury PR, McKay RT, **Carson A**, Morrison JA, Wiot JF and Spitz HB. "Pulmonary changes after exposure to vermiculite contaminated with fibrous tremolite" Am Rev Respir Dis. 129(6):952-8, 1984.

Lockey JE, Jarabek A, **Carson A**, McKay R, Harber P, Khoury P, Morrison J, Wiot J, Spitz H and Brooks SM, "Pulmonary Hazards from Vermiculite," in Health Issues Related to Metal and Nonmetallic Mining, WL Wagner, W Rom and P Merchant eds. 1983, Butterworth's, Boston.

Vinegar A and **Carson A**, "Pulmonary Function Changes in Chinese Hamsters Exposed Six Months to Diesel Exhaust," Environ Int, 5:369-371, 1981.

Lockey JE, Jarabek A, **Carson A**, McKay R, Harber P,. Khoury P, Morrison J, Prior J and Brooks SM, "Health Effects of Vermiculite Exposure," Am Rev Respir Dis, 123:133, 1981 abstract.

Lockey JE, Jarabek A, **Carson A**, McKay R, Harber P, Khoury P, Morrison J and Brooks SM, "Single-Breath Diffusing Capacity (DLCOsb) in a Working Population," Am Rev Respir Dis, 123:132, 1981 abstract.

Vinegar A, **Carson A** and Pepelko WE, "Pulmonary Function Changes in Chinese Hamsters Exposed to Diesel Exhaust," in Health Effects of Diesel Engine Emissions, Vol. 2, WE Pepelko, RM Danner and NA Clarke eds, 1980, US Environmental Protection Agency, Washington.

**Carson A**, Vinegar A, Leng J and Cooper G, "Effects of Chronic Exposure to some Diesel Exhaust Components on Lung Function in Rats," Fed Proc, 39:1091, 1980 abstract.

Elia VJ, Anderson LA, MacDonald TJ, **Carson A**, Buncher CR and Brooks SM, "Determination of Urinary Mandelic and Phenylglyoxylic Acids in Styrene Exposed Workers and a Control Population," Am Ind Hyg Assoc J, 41:922-926, 1980.

Brooks SM, Anderson LA, Emmett E, **Carson A**, Tsay JY, Elia VJ, Buncher CR and Karbowsky R, "The Effects of Protective Equipment on Styrene Exposure in Workers in the Reinforced Plastics Industry," Arch Environ Health, 35:287-294, 1980.

Brooks SM, Zipp T, Barber M and **Carson A**, "Measurement of Maximal Expiratory Flow Rates in Cigarette Smokers Using Gases of High and Low Densities," Am Rev Respir Dis, 118:75-81, 1978.

# Exhibit B

**LITERATURE:**

"A Survey of the Long-Term Effects of Talc and Kaolin Pleurodesis." *British Journal of Diseases of the Chest* 73 (1979): 285–88.

Acencio, Milena M. P., Evaldo Marchi, Lisete R. Teixeira, Bruna Rocha Silva, Juliana Sanchez Silva, Carlos Sergio Rocha Silva, Vanessa Adelia Alvarenga, Leila Antonangelo, Francisco Suso Vargas, and Vera Luiza Capelozzi. "Talc Particles and Pleural Mesothelium Interface Modulate Apoptosis and Inflammation." *Pathology* 46, no. S2 (2014): S76.

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Akhtar, Mohd Javed, Maqusood Ahamed, M.A. Majeed Khan, Salman A. Alrokayan, Iqbal Ahmad, and Sudhir Kumar. "Cytotoxicity and Apoptosis Induction by Nanoscale Talc Particles from Two Different Geographical Regions in Human Lung Epithelial Cells." *Environmental Toxicology* 29 (2014): 394–406.

Akhtar, Mohd Javed, Sudhir Kumar, Ramesh Chandra Murthy, Mohd Ashquin, Mohd Imran Khan, Govil Patil, and Iqbal Ahmad. "The Primary Role of Iron-Mediated Lipid Peroxidation in the Differential Cytotoxicity Caused by Two Varieties of Talc Nanoparticles on A549 Cells and Lipid Peroxidation Inhibitory Effect Exerted by Ascorbic Acid." *Toxicology in Vitro: An International Journal Published in Association with BIBRA* 24, no. 4 (June 2010): 1139–47.

American Cancer Society. "Key Statistics for Ovarian Cancer."

American Cancer Society. "What Is Ovarian Cancer?,"

Anderson, Garnet L., Howard L. Judd, Andrew M. Kaunitz, David H. Barad, Shirley A. A. Beresford, Mary Pettinger, James Liu, S. Gene McNeeley, Ana Maria Lopez, and Women's Health Initiative Investigators. "Effects of Estrogen plus Progestin on Gynecologic Cancers and Associated Diagnostic Procedures: The Women's Health Initiative Randomized Trial." *JAMA* 290, no. 13 (October 1, 2003): 1739–48.

Antoniou, A., P. D. P. Pharoah, S. Narod, H. A. Risch, J. E. Eyfjord, J. L. Hopper, N. Loman, et al. "Average Risks of Breast and Ovarian Cancer Associated with BRCA1 or BRCA2 Mutations Detected in Case Series Unselected for Family History: A Combined Analysis of 22 Studies." *American Journal of Human Genetics* 72, no. 5 (May 2003): 1117–30.

Arellano-Orden, Elena, Auxiliadora Romero-Falcon, Jose Martin Juan, Manuel Ocana Jurado, Francisco Rodriguez-Panadero, and Ana Montes-Worboys. "Small Particle-Size Talc Is Associated with Poor Outcome and Increased Inflammation in Thoracoscopic Pleurodesis." *Respiration* 86 (2013): 201–9.

Armstrong, Deborah K., Brian Bundy, Lari Wenzel, Helen Q. Huang, Rebecca Baergen, Shashikant Lele, Larry J. Copeland, Joan L. Walker, Robert A. Burger, and Gynecologic Oncology Group. "Intraperitoneal Cisplatin and Paclitaxel in Ovarian Cancer." *The New England Journal of Medicine* 354, no. 1 (January 5, 2006): 34–43.

"ATSDR - Toxicological Profile: Asbestos." Accessed August 16, 2018.

Baldwin, Lauren A., Bin Huang, Rachel W. Miller, Thomas Tucker, Scott T. Goodrich, Iwona

Podzielinski, Christopher P. DeSimone, Fred R. Ueland, John R. van Nagell, and Leigh G. Seamon. "Ten-Year Relative Survival for Epithelial Ovarian Cancer:" *Obstetrics & Gynecology* 120, no. 3 (September 2012): 612–18.

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**DEPOSITIONS, TRANSCRIPTS AND REPORTS:**

Affidavit of Laura Plunkett, PhD 02.22.18

Deposition of Alice Blount in the Ingham v. J&J Matter on 04.13.18

Deposition of Annie Awanais Yessian on 07.13.2017

Deposition and Exhibits of Pat Downey Dated 8.7.18-8.8.18
Deposition and Exhibits of John Hopkins Dated 8.16.18-8.17.18, 10.17.18 and 11.05.18
Deposition and Exhibits of Susan Nicholson Dated 7.26.18-7.27.18
Deposition and Exhibits of Julie Pier Dated 9.12.18-9.13.18
Ingham v. J&J Volume 11 (Egilman, Koman, Martinez, Packard) 6-14-18
Ingham v. J&J Volume 14A (Madigan, Williams) 6-20-18
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Ingham v. JJ Volume 24B (Warner Huh, MD) 7.5.18
John J. Godleski Expert Report for Brower Matter Dated 6.23.18
Lanzo Plaintiffs MIL re Imerys Spoliation and Concealment of Talc Samples
Laura Plunkett - Supplemental Expert Brower Report
Longo Analysis of J&J's Historical Talc Samples from the 1960's
Longo Analysis of J&J's Historical Talc Samples from the 1970's
Longo Analysis of J&J's Historical Talc Samples from the 1980's
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Longo Analysis of J&J's Baby Powder Historical Samples - Asian - October 2018
Longo Analysis of J&J's BP Talc Products for Amphibole (Tremolite) Asbestos 8.2.17
Longo Analysis Report_Exhibit BB_04.28.2017
Longo MAS Project 14-1852 Below the Waist Application of Johnson's BP 9.2017
Longo Process Blanks for the Analysis of J&J's Products from the 60's to 90's for Asbestos
Longo TEM Analysis of Historical 1978 Johnson's BP Sample for Amphibole Asbestos 2.16.18
Longo Verification of Lee Poye's TEM Analysis of J&J's Historical Vermont Talc 11.5.18
Michael Crowley Expert Report Dated 11.12.18
Report of Results: MVA11730 Investigation of Italian Talc Samples for Asbestos 08.01.2017
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Thomas Dydek Brower Expert Report Dated 8.16.18 (corrected on 8.20.18)
Thomas Dydek Educational Report_FINAL (4-9-2018)
Thomas Dydek MDL Educational Report Dated 4.9.18

**OTHER SOURCES:**

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EPA Guidelines for Carcinogen Risk Assessment - March 2005
EPA Health Assessment Document for Talc - 1992
Exhibit 1 - ATTORNEYS' EYES ONLY
Exhibit 2 - ATTORNEYS' EYES ONLY
Exhibit 3 - ATTORNEYS' EYES ONLY
FDA 4-1-2014 Response Letter to Epstein Denying Petition
Fitzgerald Analysis of J&J Baby Powder #1 and #2 Dated July 26, 2017
IARC Monograph 100C - Arsenic, Metals, Fibres, and Dusts - Excerpts
IARC Monograph 14 - Asbestos - 1977

IARC Monograph 2 - Some Inorganic and Organometallic Compounds - 1973
IARC Monograph 68 - Silica, Some Silicates, Coal Dust and Para-Aramid Fibrils - 1997
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J&J History
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Read-the-Letter-from-the-FDA-on-Cosmetics
The Birth of Our Baby Products _ Kilmer House
WCD 002478 - Exhibit 32 Waldstreicher

**Arch Carson, MD, PhD Legal Testimony, 2015-2018**

Elaine Hale and Kenneth Dorsey parker, Jr. v. Centerpoint Energy Houston Electric, LLC; in the 55th District Court of Harris County, Texas.
2016 Harris County, TX for Plaintiff

Danny Henderson and Linda Henderson; Magdaleno Flores and Maria Flores; Shari Waldrop; and Bryan Thomas v. Magnablend, Inc., Nugreen Specialty, Inc., Nugreen Solutions, Inc., and Enviro Tech Inc.; in the 40th District Court of Ellis County, Texas.
2015 Ellis County, TX for Defendant

Edgar Guadalupe Solis v. Eastman Chemical Company, Texas Operations, Tradebe Environmental Services, Inc. d/b/a Tradebe Industrial Services LLC; in the 234th District Court of Harris County, Texas.
2015 Harris County, TX for Defendant

Arch I. Carson, MD, PhD
Professional Consultation Fee Schedule

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| Evidence-base research, report preparation, documentation, conference | $450/hr |
| Interview, physical examination or medical testing of patients | 450/hr |
| Review of documents | 450/hr |
| Testimony at deposition or trial plus expenses | 450/hr |
| Inspection, examination or sampling of physical evidence or sites | 450/hr |
| Travel<br>(Travel maximum $4,000 per diem, plus expenses) | 200/hr |
| Laboratory analyses/studies | at cost |
| Overhead and Supplies | at cost |